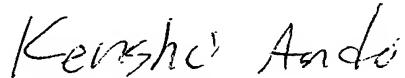


VERIFICATION OF TRANSLATION

I, Kenshi ANDO, a Japanese Patent Attorney, Registration No. 13721 having my business office at Kitanomaru Square 1-13-12, Kudankita, Chiyoda-ku, Tokyo 102-8667, Japan, do hereby certify:

1. That I am familiar with the Japanese language and the English language; and
2. That, to the best of my knowledge and belief, the attached document represents a true and correct English language translation of the certified copy of Japanese Patent application No. JP2003-184879, Reference No. BY0026PV, which was filed with the Japan Patent Office on June 27, 2003.

Signed at Tokyo, Japan, this 25 day of September, 2007.



Kenshi ANDO

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[Indication of Fee]

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[List of Submitted Articles]

[Name of Article] Specification 1

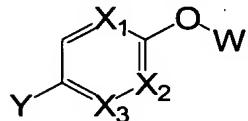
[Name of Article] Abstract 1

[Designation of Document] Specification

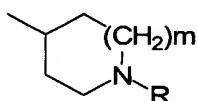
[Title of the Invention] HETEROARYLOXY-NITROGEN-CONTAINING SATURATED HETEROCYCLIC DERIVATIVES

5 [CLAIMS]

1. A compound of the following formula (I) or its pharmaceutically-acceptable salt:



(I)

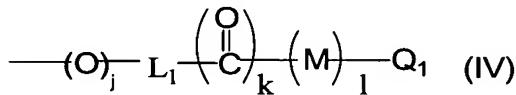
[wherein X^1 , X^2 and X^3 each independently represent N or CH (provided that all of X^1 , X^2 and X^3 are not CH at the same time); W represents a group of the following formula (II):

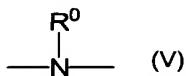
10 (II)

(wherein m indicates an integer of from 0 to 3; R represents a linear or branched lower alkyl group (excepting a methyl group), a cycloalkyl group having from 3 to 9 carbon atoms, an aralkyl group or a heterocyclic group having from 3 to 8 carbon atoms (the hetero ring has 1 or 2 nitrogen atoms or oxygen atoms), which may be substituted with a group selected from a class consisting of a cyano group, a 15 hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxyl group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a cycloalkyliminocarbonyl group and a trifluoromethyl group), or represents a group of 20 a formula (III):

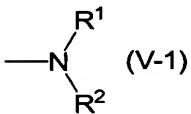


(III)

(wherein m^1 indicates an integer of from 0 to 3; n indicates an integer of from 0 to 2); Y represents a group of a formula (IV):25 (wherein j, k and l each independently indicate 0 or 1; L_1 represents a lower alkylene group having from 1 to 4 carbon atoms, or a single bond; M represents an oxygen atom or a group of a formula (V):



(wherein R^0 represents a lower alkyl group having from 1 to 4 carbon atoms); Q_1 represents a linear or branched lower alkyl group, a cycloalkyl group having from 3 to 9 carbon atoms, a phenyl group, a 5-membered or 6-membered heteroaryl group, a heterocyclic group having from 3 to 8 carbon atoms (the hetero ring has 1 or 2 nitrogen atoms or oxygen atoms), a naphthyl group or a condensed-cyclic heteroaryl group, which may be substituted with a group selected from a class consisting of a cyano group, a hydroxy group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower alkylsulfonyl group, a cyclo-lower alkylsulfonyl group, a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a trifluoromethyl group, a mono-lower alkylamino group, a di-lower alkylamino group, an alkanoyl group, an alkoxy carbonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), an alkanoylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group) and an alkylsulfonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), or represents a group of a formula (V-1):



(wherein R^1 and R^2 are the same or different, each representing a lower alkyl group or a mono- or di-lower alkylcarbamoyl group, or R^1 and R^2 together form, along with the adjacent nitrogen atom, a 3- to 9-membered lactam ring, a heterocyclic group having from 3 to 8 carbon atoms (the group has 1 or 2 nitrogen atoms or oxygen atoms), a 5-membered heteroaryl group, or a condensed-cyclic heteroaryl group)].

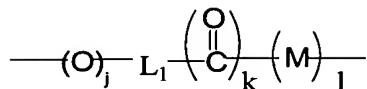
2. The compound as claimed in claim 1, wherein R in formula (II) is a cycloalkyl group having from 3 to 9 carbon atoms or a heterocyclic group having from 3 to 8 carbon atoms (the hetero ring has 1 or 2 nitrogen atoms or oxygen atoms), which may be substituted with a group selected from a class consisting of a cyano group, a hydroxy group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group, a mono-lower alkylaminocarbonyloxy group and a di-lower alkylaminocarbonyloxy group, or a represents a group of a formula (III):



(III)

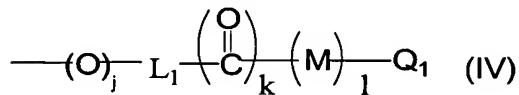
[wherein m_1 indicates an integer of from 0 to 3; and n indicates an integer of from 0 to 2].

3. The compound as claimed in claim 1 or 2, wherein the group of formula (IV-1):

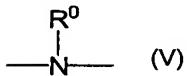


(IV-1)

(wherein the symbols have the same meanings as above) in formula (IV):

[wherein j, k and l each independently indicate 0 or 1; L₁ represents a lower alkylene group having from 1

5 to 4 carbon atoms, or a single bond; M represents an oxygen atom, or a group of a formula (V):

(wherein R⁰ represents a lower alkyl group having from 1 to 4 carbon atoms); Q₁ represents a linear or branched lower alkyl group, a cycloalkyl group having from 3 to 9 carbon atoms, a phenyl group, a 5-membered or 6-membered heteroaryl group, a heterocyclic group having from 3 to 8 carbon atoms (the hetero ring has 1 or 2 nitrogen atoms or oxygen atoms), a naphthyl group or a condensed-cyclic

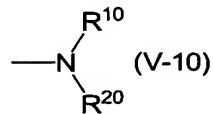
10 heteroaryl group, which may be substituted with a group selected from a class consisting of a cyano group, a hydroxy group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower alkylsulfonyl group, a cyclo-lower alkylsulfonyl group, a halogen atom, a mono-lower 15 alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a trifluoromethyl group, a mono-lower alkylamino group, a di-lower alkylamino group, an alkanoyl group, an alkoxy carbonyl amino group (the nitrogen atom in the group may be substituted with a lower alkyl group), an alkanoyl amino group (the nitrogen atom in the group may be substituted with a lower alkyl group) and an alkylsulfonyl amino group (the nitrogen atom in the group may be substituted with a lower alkyl group)] is

20 a C₁₋₄ lower alkylene group, a carbonyl group, -C(O)-O-, a -C₁₋₄ lower alkylene-C(O)-, a -C₁₋₄ lower alkylene-C(O)-O-, a -C₁₋₄ lower alkylene-C(O)-N(R⁰)-, -C(O)-N(R⁰)-O-, -O-C₁₋₄ lower alkylene-, or a single bond.25 4. The compound as claimed in claim 3, wherein Q₁ is a linear or branched lower alkyl group, a cycloalkyl group having from 3 to 9 carbon atoms, a phenyl group or a naphthyl group, which may be substituted with a group selected from a class consisting of a cyano group, a hydroxy group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower 30 alkylsulfonyl group, a cyclo-lower alkylsulfonyl group, a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a trifluoromethyl group, a mono-lower alkylamino group, a di-lower alkylamino group, an alkanoyl

group, an alkoxy carbonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), an alkanoylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group) and an alkylsulfonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), or represents a 5- or 6-membered heteroaryl group having from 1 to 3 hetero atoms

5 selected from a group consisting of an oxygen atom, a sulfur atom and a nitrogen atom, a heterocyclic group having from 3 to 8 carbon atoms and having from 1 to 3 nitrogen atoms or oxygen atoms in the ring, or a mono- to tri-cyclic condensed-cyclic heteroaryl group optionally having from 1 to 3 hetero atoms selected from a group consisting of an oxygen atom, a sulfur atom and a nitrogen atom in each ring.

10 5. The compound as claimed in claim 3, wherein Q_1 of formula (V-1) is a group of a formula (V-10):



[wherein R^{10} and R^{20} together form, along with the adjacent nitrogen atom, a 3- to 9-membered lactam ring, a heterocyclic ring having from 3 to 8 carbon atoms (R^{10} and R^{20} may have, apart from the adjacent nitrogen atom, 1 or 2 nitrogen atoms or oxygen atoms in the ring as the constitutive atoms of the hetero ring), a 5-membered heteroaryl group having from 1 to 4 nitrogen atoms in the ring, or a bicyclic condensed-cyclic heteroaryl group having from 1 to 3 nitrogen atoms or oxygen atoms in each ring].

15 6. The compound as claimed in claim 1, wherein -Y in formula (I) is a phenyl group, a pyridyl group, a pyridazinyl group or a pyrimidinyl group, which may be substituted with a group selected from a class consisting of a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower alkylsulfonyl group, a cyclo-lower alkylsulfonyl group, a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a mono-lower alkylamino group, a di-lower alkylamino group, an alkanoyl group, an alkoxy carbonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), an alkanoylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group) and an alkylsulfonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group).

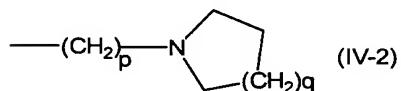
20 7. The compound as claimed in claim 1, wherein -Y in formula (I) is a bi- or tri-cyclic condensed ring having at least one phenyl group or pyridyl group in the ring, which may have therein 1 or 2 substituents selected from a class consisting of a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower alkylsulfonyl group, a cyclo-lower alkylsulfonyl group, a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a mono-lower alkylamino group, a di-lower alkylamino

group, an alkanoyl group, an alkoxycarbonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), an alkanoylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group) and an alkylsulfonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group).

5 8. The compound as claimed in claim 1, wherein -Y in formula (I) is a furyl group, a thienyl group, a pyrrolyl group, an imidazolyl group, a pyrazolyl group, a thiazolyl group, a thiadiazolyl group, an isothiazolyl group, an oxazolyl group, an isoxazolyl group, a pyridyl group, a pyridazinyl group, a pyrimidinyl group or a pyrazinyl group, which may have in the ring thereof, 1 or 2 substituents selected from a class consisting of a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower alkylsulfonyl group, a cyclo-lower alkylsulfonyl group, a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a mono-lower alkylamino group, a di-lower alkylamino group, an alkanoyl group, an alkoxycarbonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), an alkanoylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group) and an alkylsulfonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group).

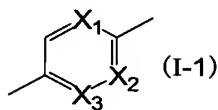
20 9. The compound as claimed in claim 1, wherein -Y in formula (I) is an oxetanyl group, a tetrahydrofuranyl group, a tetrahydropyranyl group, a pyrrolidinyl group, a piperidinyl group, a homopiperidinyl group, a morpholinyl group or a homomorpholinyl group, which may have in the ring thereof, 1 or 2 substituents selected from a class consisting of a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a mono-lower alkylamino group, a di-lower alkylamino group, an alkanoyl group, an alkoxycarbonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), an alkanoylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group) and an alkylsulfonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group).

25 10. The compound as claimed in claim 1, wherein -Y in formula (I) is a group of a formula (IV-2):



30 35 (wherein p indicates an integer of from 1 to 3; q indicates an integer of from 1 to 4).

11. The compound as claimed in any of claims 1 to 10, wherein at least one of X¹ and X² in the group of formula (I-1):



[wherein X^1 , X^2 and X^3 each independently represent N or CH (provided that all of X^1 , X^2 and X^3 are not CH at the same time)] is a nitrogen atom, or both X^2 and X^3 therein are nitrogen atoms.

12. The compound of formula (I) as claimed in any of claims 1 to 11, which includes

5 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,
 2-(1-isopropylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,
 2-(1-cyclopentylpyrrolidin-3-yloxy)-5-(4-carbamoylphenyl)pyrimidine,
 2-(1-cyclopentylpyrrolidin-3-yloxy)-5-(4-cyanophenyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{(4-methyl-1,3,5-oxadiazol-2-yl)phenyl}pyrimidine,
 10 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,
 2-(1-cyclobutylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,
 2-(1-cyclohexylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,
 2-(1-cyclopropylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,
 2-(1-ethylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,
 15 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(pyrrolidin-1-ylcarbonyl)phenyl}piperidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(dimethylcarbamoyl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(morpholin-4-ylcarbonyl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(phenoxy)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(3-quinolinyl)pyrimidine,
 20 2-(1-cyclopentylpiperidin-4-yloxy)-5-(5-indolyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(pyridon-1-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(piperidon-1-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(3-quinolinyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-phenyl-4-hydroxypiperidin-1-yl)pyrimidine,
 25 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-methoxypyridin-5-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-chlorophenyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-trifluoromethylphenyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(3-pyridinyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-methoxyphenyl)pyrimidine,
 30 2-(1-cyclopentylpiperidin-4-yloxy)-5-(dibenzofuran-4-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-cyclopentyloxypyridin-5-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-pyridon-5-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(1-cyclopentyl-2-pyridon-3-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{2-(pyrrolidin-1-ylcarbonyl)pyridin-5-yl}pyrimidine,
 35 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-cyano-5-thenyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(oxomorpholin-4-yl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(2-oxazolidin-3-yl)phenyl}pyrimidine,

2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-methyl-3-pyridin-5-yl)pyrimidin,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-fluoro-3-pyridin-5-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(2-pyridon-1-yl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(methylsulfonyl)phenyl}pyrimidine,
 5 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-acetylphenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-trifluoromethoxyphenyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(2-hydroxy-2-propyl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-ethylpyridin-5-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrazine,
 10 5-(1-cyclopentylpiperidin-4-yloxy)-2-(4-cyanophenyl)pyridine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyridazine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(piperidin-1-ylcarbonyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(piperidin-1-ylmethyl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-phenylpiperazin-1-ylmethyl)pyrimidine,
 15 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-cyanopyrimidin-5-yl)pyrimidine.

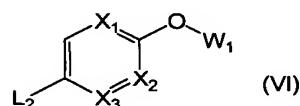
13. A histamine-H3 receptor antagonist or inverse-agonist containing, as the active ingredient thereof, a compound of any of claims 1 to 12.

14. A histamine-H3 receptor antagonist containing, as the active ingredient thereof, a compound of any of claims 1 to 12.

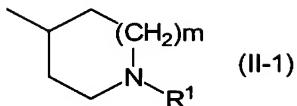
20 15. A histamine-H3 receptor inverse-agonist containing, as the active ingredient thereof, a compound of any of claims 1 to 12.

16. A preventive or remedy comprising, as the active ingredient thereof, a compound of any of claims 1 to 7, which is for metabolic system diseases such as obesity, diabetes, hormone secretion disorder, hyperlipemia, gout, and fatty liver; circulatory system diseases, for example, stenocardia, 25 acute/congestive cardiac insufficiency, cardiac infarction, coronary arteriosclerosis, hypertension, nephropathy, and central and peripheral nervous system diseases such as bulimia, emotional disorder, melancholia, anxiety, epilepsy, delirium, dementia, shinzoephrenia, attention deficit/hyperactivity disorder, memory disorder, Alzheimer's disease, Parkinson's disease, sleep disorder, recognition disorder, motion disorder, paresthesia, dysosmia, epilepsy, morphine resistance, narcotic dependency, and alcoholic dependency.

30 17. A method for producing a compound of a general formula (I-2) or a compound of a general formula (I-3) or a salt thereof, which comprises reacting a compound of a general formula (VI):



[wherein X¹, X² and X³ each independently represent N or CH (provided that all of X¹, X² and X³ are not CH at the same time); W¹ represents a group of the following formula (II-1):



(wherein m indicates an integer of from 0 to 3; R¹ represents a linear or branched lower alkyl group (excepting a methyl group), a cycloalkyl group having from 3 to 9 carbon atoms, an aralkyl group or a heterocyclic group having from 3 to 8 carbon atoms (the hetero ring has 1 or 2 nitrogen atoms or oxygen atoms), which may be substituted with a group selected from a class consisting of a cyano group, a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxyl group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a cycloalkyliminocarbonyl group and a trifluoromethyl group, or represents a group corresponding to R but having a protective group suitably introduced into the substituent which R has), or represents a group or a formula (III):

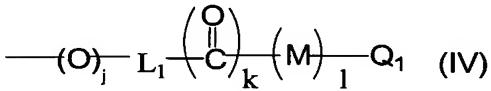


(III)

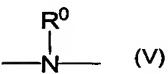
(wherein m₁ indicates an integer of from 0 to 3; n indicates an integer of from 0 to 2); and L₃ represents a leaving group], with a compound of a general formula (XI):

Met—Y^{1p} (XI)

[wherein Met represents a general organic metal atom; Y^{1p} represents a group of a formula (IV):



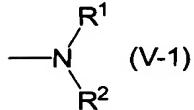
(wherein j, k and l each independently indicate 0 or 1; L₁ represents a lower alkylene group having from 1 to 4 carbon atoms, or a single bond; M represents an oxygen atom or a group of a formula (V):



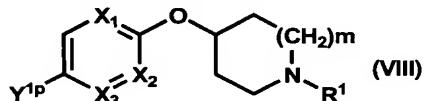
(wherein R⁰ represents a lower alkyl group having from 1 to 4 carbon atoms); Q₁ represents a linear or branched lower alkyl group, a cycloalkyl group having from 3 to 9 carbon atoms, a phenyl group, a 5-membered or 6-membered heteroaryl group, a heterocyclic group having from 3 to 8 carbon atoms (the hetero ring may have 1 or 2 nitrogen atoms or oxygen atoms), a naphthyl group or a condensed-cyclic heteroaryl group, which may be substituted with a group selected from a class consisting of a cyano group, a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxyl group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower alkylsulfonyl group, a cyclo-lower alkylsulfonyl group, a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower

alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a trifluoromethyl group, a mono-lower alkylamino group, a di-lower alkylamino group, an alkanoyl group, an alkoxycarbonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), an alkanoylamino group (the nitrogen atom in the group may be

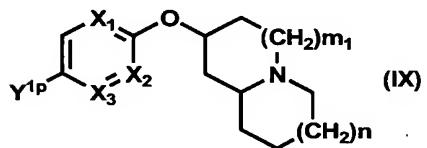
5 substituted with a lower alkyl group) and an alkylsulfonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), or represents a group corresponding to Q_1 but having a protective group optionally introduced into the substituent which Q_1 has, or represents a group of a formula (V-1):



10 (wherein R¹ and R² are the same or different, each representing a lower alkyl group or a mono- or di-lower alkylcarbamoyl group, or R¹ and R² together form, along with the adjacent nitrogen atom, a 3- to 9-membered lactam ring, a heterocyclic group having from 3 to 8 carbon atoms (the group has 1 or 2 nitrogen atoms or oxygen atoms in the ring thereof), a 5-membered heteroaryl group or a condensed-cyclic heteroaryl group), or represents a group corresponding to -Y but having a protective group optionally introduced into the substituent which -Y has), in the presence of a catalyst, to give a compound of a general formula (VIII):

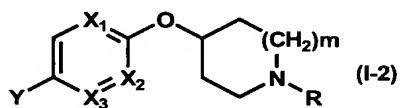


[wherein X^1 , X^2 , X^3 , m , R^1 and Y^{1p} have the same meanings as above], or a compound of a general formula (IX):

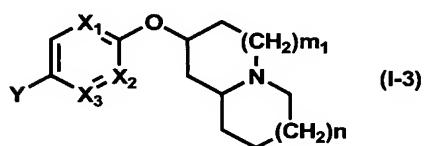


20

[wherein X^1 , X^2 , X^3 , m_1 , n and Y^{1p} have the same meanings as above], and optionally removing the protective group to give a compound of a general formula (I-2):

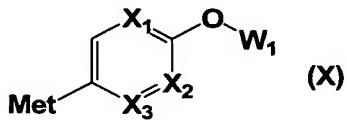


[wherein X^1 , X^2 , X^3 , m , R and Y have the same meanings as above], or a compound of a general formula (I-3):

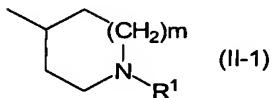


[wherein X^1 , X^2 , X^3 , m_1 , n and Y have the same meanings as above], or a salt thereof.

18. A method for producing a compound of a general formula (I-2) or a compound of a general formula (I-3) or a salt thereof, which comprises reacting a compound of a general formula (X):



[wherein X^1 , X^2 and X^3 each independently represent N or CH (provided that all of X^1 , X^2 and X^3 are not CH at the same time); W^1 represents a group of the following formula (II-1):



(wherein m indicates an integer of from 0 to 3; R^1 represents a linear or branched lower alkyl group (excepting a methyl group), a cycloalkyl group having from 3 to 9 carbon atoms, an aralkyl group or a heterocyclic group having from 3 to 8 carbon atoms (the hetero ring has 1 or 2 nitrogen atoms or oxygen atoms), which may be substituted with a group selected from a class consisting of a cyano group, a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxyl group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a cycloalkyliminocarbonyl group and a trifluoromethyl group), or represents a group corresponding to R but having a protective group suitably introduced into the substituent which R has, or represents a group or a formula (III):

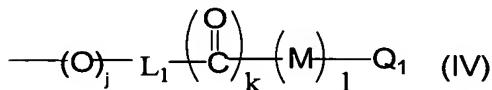


(III)

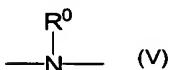
(wherein m_1 indicates an integer of from 0 to 3; n indicates an integer of from 0 to 2); and Met represents a general organic metal atom], with a compound of a general formula (XI):



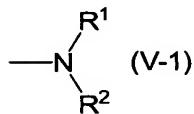
[wherein L_2 represents a leaving group; Y^{1p} represents a group of a formula (IV):



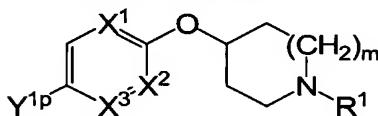
(wherein j, k and 1 each independently indicate 0 or 1; L_1 represents a lower alkylene group having from 1 to 4 carbon atoms, or a single bond; M represents an oxygen atom or a group of a formula (V):



(wherein R^0 represents a lower alkyl group having from 1 to 4 carbon atoms); Q_1 represents a linear or branched lower alkyl group, a cycloalkyl group having from 3 to 9 carbon atoms, a phenyl group, a 5-membered or 6-membered heteroaryl group, a heterocyclic group having from 3 to 8 carbon atoms (the hetero ring has 1 or 2 nitrogen atoms or oxygen atoms), a naphthyl group or a condensed-cyclic heteroaryl group, which may be substituted with a group selected from a class consisting of a cyano group, a hydroxy group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower alkylsulfonyl group, a cyclo-lower alkylsulfonyl group, a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a trifluoromethyl group, a mono-lower alkylamino group, a di-lower alkylamino group, an alkanoyl group, an alkoxy carbonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), an alkanoylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group) and an alkylsulfonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), or represents a group corresponding to Q_1 but having a protective group optionally introduced into the substituent which Q_1 has, or represents a group of a formula (V-1):

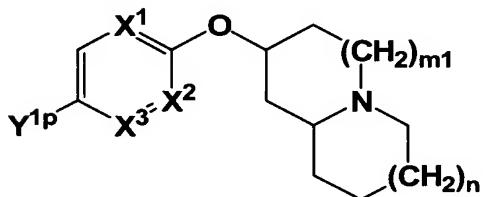


(wherein R^1 and R^2 are the same or different, each representing a lower alkyl group or a mono- or di-lower alkylcarbamoyl group, or R^1 and R^2 together form, along with the adjacent nitrogen atom, a 3- to 9-membered lactam ring, a heterocyclic group having from 3 to 8 carbon atoms (the group has 1 or 2 nitrogen atoms or oxygen atoms in the ring thereof), a 5-membered heteroaryl group or a condensed-cyclic heteroaryl group), or represents a group corresponding to -Y but having a protective group optionally introduced into the substituent which -Y has], in the presence of a catalyst, to give a compound of a general formula (XII):



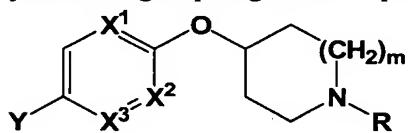
(XII)

(wherein X^1 , X^2 , X^3 , m , R^1 and Y^{1p} have the same meanings as above), or a compound of a general formula (XIII):



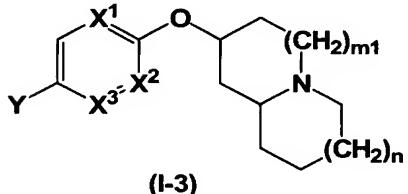
(XIII)

(wherein X^1 , X^2 , X^3 , m , n and Y^{1p} have the same meanings as above), and optionally removing the protective group to give a compound of a general formula (I-2):



(I-2)

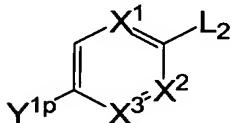
(wherein X^1 , X^2 , X^3 , m , R and Y have the same meanings as above), or a compound of a general formula 5 (I-3):



(I-3)

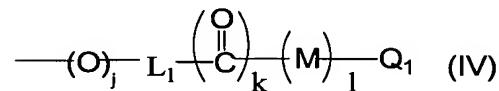
(wherein X^1 , X^2 , X^3 , m , n and Y have the same meanings as above), or a salt thereof.

19. A method for producing a compound (I) of the invention, which comprises reacting a compound of a general formula (XIV):

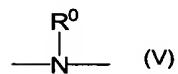


(XIV)

[wherein X^1 , X^2 and X^3 each independently represent N or CH (provided that all of X^1 , X^2 and X^3 are not CH at the same time); Y^{1p} represents a group of a formula (IV):

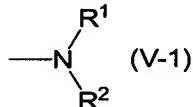


(wherein j , k and l each independently indicate 0 or 1; L_1 represents a lower alkylene group having from 1 to 4 carbon atoms, or a single bond; M represents an oxygen atom or a group of a formula (V):



(wherein R^0 represents a lower alkyl group having from 1 to 4 carbon atoms); Q_1 represents a linear or branched lower alkyl group, a cycloalkyl group having from 3 to 9 carbon atoms, a phenyl group, a 5-membered or 6-membered heteroaryl group, a heterocyclic group having from 3 to 8 carbon atoms (the hetero ring has 1 or 2 nitrogen atoms or oxygen atoms), a naphthyl group or a condensed-cyclic heteroaryl group, which may be substituted with a group selected from a class consisting of a cyano group, a hydroxy group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower alkylsulfonyl group, a cyclo-lower alkylsulfonyl group, a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower

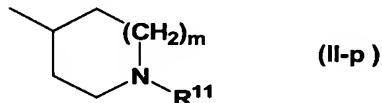
alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a trifluoromethyl group, a mono-lower alkylamino group, a di-lower alkylamino group, an alkanoyl group, an alkoxy carbonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), an alkanoylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group) and an alkylsulfonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), or represents a group corresponding to Q_1 but having a protective group optionally introduced into the substituent which Q_1 has, or represents a group of a formula (V-1):



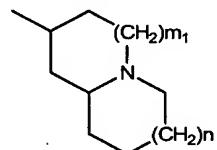
10 (wherein R^1 and R^2 are the same or different, each representing a lower alkyl group or a lower alkylcarbamoyl group having from 1 to 6 carbon atoms, or R^1 and R^2 together form, along with the adjacent nitrogen atom, a 3- to 9-membered lactam ring, a heterocyclic group having from 3 to 8 carbon atoms (the group has 1 or 2 nitrogen atoms or oxygen atoms in the ring thereof), a 5-membered heteroaryl group or a condensed-cyclic heteroaryl group), or represents a group corresponding to $-Y$ but having a protective group optionally introduced into the substituent which $-Y$ has; L_2 represents a leaving group], with a compound of a general formula (XV):



[wherein W^1 represents a group of the following formula (II-p):

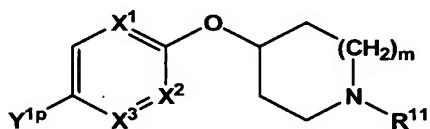


20 (wherein R^{11} is R^1 or an amino-protective group; and the other symbols have the same meanings as above), or represents a group of a formula (III):



(III)

(wherein the symbols have the same meanings as above)] or its salt to give a compound of a general formula (VI-1):



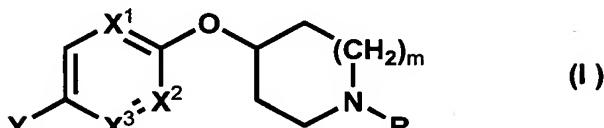
25 (XVI)

[wherein X^1 , X^2 , X^3 , Y^{1p} , m and R^{11} have the same meanings as above], and when the compound and R^{11} have a protective group for the amino group therein, then removing the amino-protective group, and

thereafter further reacting it with a precursor aldehyde or ketone corresponding to R¹ or with a compound of a general formula (XVII):



(wherein the symbols have the same meanings as above), and optionally removing the protective group to give a compound (I) of the invention:



(wherein the symbols have the same meanings as above].

[Description]

[Technical Field]

10 The present invention relates to heteroaryloxy-nitrogen-containing saturated heterocyclic derivatives useful in the field of medicines. The compounds act as a histamine-H3 receptor antagonist, and are useful for preventives or remedies for various circulatory system disorders, nervous system disorders, metabolic system disorders, etc.

[background art]

15 It has been known that, in organisms such as typically mammals, histamine that is a physiologically-active endogenous factor functions as a neurotransmitter and has extensive pharmacological activities (for example, non patent reference 1). Immunohistochemical studies have made it clear that a histamine-agonistic (producing) cell body exists in the nodal papillary nucleus in a posterior hypothalamic region and that histamine nerve fibers project in an extremely broad range in the 20 brain, which supports various pharmacological effects of histamine (for example, non patent reference 2).

The existence of histamine-agonistic nerves in the nodal papillary nucleus in a posterior hypothalamic region suggests that histamine may have an important role in control of physiological functions relating to brain functions, especially to hypothalamic functions (sleep, vigilance rhythm, incration, eating and drinking action, sexual action, etc.) (for example, non patent reference 3).

25 The existence of projection to the brain region that relates to vigilance sustenance, for example, to cerebral cortex suggests the role in control of vigilance or vigilance-sleep cycle. The existence of projection to many peripheral structures such as hippocampus and amygdaloid complex suggests the role in control of autonomic nerves, emotion, control of motivated action and learning/memory process.

30 When released from producing cells, histamine acts with a specific polymer that is referred to as a receptor on the surface of a cell membrane or inside a target cell, therefore exhibiting its pharmacological effects for control of various body functions. Heretofore, four types of histamine receptors have been found. In particular, the presence of a histamine receptor that participates in the central and peripheral nervous functions, histamine-H3 receptor, has been shown by various pharmacological and physiological studies (for example, non patent reference 4); and recently, human and 35 rodent histamine-H3 receptor genes have been identified and their existence has been made clear (for example, non patent reference 5).

It is suggested that histamine-H3 receptor exists in the presynaptic membrane of central or

5 peripheral neurocytes and functions as a self-receptor, therefore controlling the release of histamine and controlling the release of other neurotransmitters. Specifically, it is reported that a histamine-H3 receptor agonist, or its antagonist or inverse-agonist controls the release of histamine, noradrenaline, serotonin, acetylcholine or dopamine from nerve ending. For example, the release of these neurotransmitters is inhibited by an agonist such as (R)-(α)-methylhistamine inhibits, and is promoted by an antagonist or inverse-agonist such as thioperamide (for example, non patent reference 6).

10 Recent studies have shown that histamine-H3 receptor has extremely high homeostatic activities (endogenous agonistic factor, e.g., activity observed in the absence of histamine) in the receptor-expressing cells/tissues or in a membrane fraction derived from the expressing cells/tissues and even in living bodies (for example, non patent reference 7). It is reported that these homeostatic activities are inhibited by an inverse-agonist. For example, a homeostatic self-receptor activity is inhibited by thioperamide or sypoxyfan, and, as a result, the release of neurotransmitters from nerve ending, for example, the release and liberation of histamine from it is thereby promoted.

15 In animal experiments with rats, a high-level selective inhibitor of histamine synthase (histidine decarboxylase) inhibits the vigilance of rats, which suggests that histamine may function for controlling motive vigilance, Administration of a histamine-H3 receptor agonist, (R)-(α)-methylhistamine to cats increases their deep slow-wave sleep (for example, non patent reference 8). Contrary to this, a histamine-H3 receptor antagonist or inverse-agonist, thioperamide dose-dependently increase vigilance. In addition, thioperamide decreases slow-wave and REM sleep (for example, non patent reference 9).

20 These pieces of information suggest that the H3 receptor may participate in vigilance-sleep control and in diseases accompanied by sleep deficiency.

In animal experiments with rats, administration of histamine to the ventricle of rats inhibited their eating action, therefore suggesting that histamine may participate in control of eating action (for example, non patent reference 10).

25 A histamine-H3 receptor antagonist or inverse-agonist, thioperamide dose-dependently inhibits eating action. In addition, thioperamide promotes intracerebral histamine release (for example, non patent reference 11). These pieces of information suggest that the H3 receptor may participate in eating action control, further suggesting a possibility that an H3 antagonist or inverse-agonist may be useful for prevention or remedy of metabolic diseases such as eating disorder, obesity, diabetes, emaciation, 30 hyperlipemia.

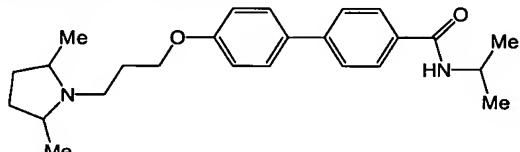
35 In animal experiments with rats, administration of a histamine-H3 receptor agonist, (R)-(α)-methylhistamine to rats dose-dependently lowered their basal diastolic pressure. Its action was antagonized by a histamine-H3 receptor antagonist or inverse-agonist, thioperamide (for example, non patent reference 12). These pieces of information suggest that a histamine-H3 receptor may participate in control of blood pressure, heart beat and cardiac output, further suggesting a possibility that a histamine-H3 receptor agonist or its antagonist or inverse-agonist may be useful for prevention or remedy of circulatory system diseases such as hypertension and various cardiac disorders.

In animal experiments with rats, administration of a histamine-H3 receptor agonist, (R)-(α)-methylhistamine to rats lowered their object recognition and learning effects in the object

recognition test and the passive turnout test with them. On the other hand, in the scopolamine-induced amnesia test with them, a histamine-H3 receptor antagonist or inverse-agonist, thioperamide dose-dependently relieved their amnesia induced by the chemical (for example, non patent reference 13). These pieces of information suggest a possibility that a histamine-H3 receptor antagonist or inverse-agonist may be useful for prevention or remedy of various diseases accompanied by memory and learning disorder, for example, Alzheimer's disease, Parkinson's disease or attention deficit/hyperactivity disorder.

It is shown that, in animal experiments with rats, a histamine-H3 receptor antagonist or inverse-agonist, thioperamide dose-dependently inhibited the spasm induced by electric shock or the epileptoid seizure induced by pentylenetetrazole (PTZ) (for example, non patent reference 14 and non patent reference 15). These pieces of information suggests a possibility that a histamine-H3 receptor antagonist or inverse-agonist may be useful for prevention or remedy of epilepsy or central spasm.

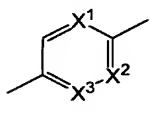
In addition to the above-mentioned thioperamide or cycloxyfan, for example, a compound of the following formula (A):



(A)

is described as a histamine-H3 receptor-antagonistic or inverse-agonistic compound (patent reference 1).

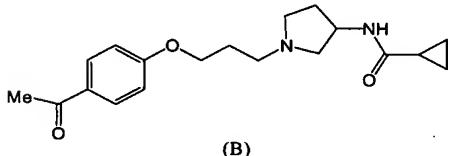
The compound of formula (A) has a propylene group between the pyrrolidinyl group and the oxygen atom therein, and it differs from compounds (I) of the present invention in that the oxygen atom directly bonds to the pyrrolidinyl group in the latter. Further, they differ in that, in the compound of formula (A), a phenyl group bonds to the oxygen atom, but in the compounds of the present invention, a group of the following formula (I-1)



(I-1)

wherein the symbols have the same meanings as above, bonds to the oxygen atom, and at least one of X¹, X² and X³ in the ring is a nitrogen atom.

A compound of the following formula (B):

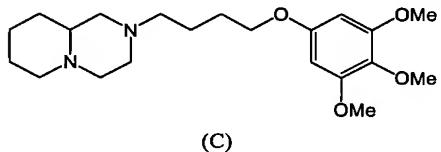


is described as a histamine-H3 receptor antagonistic compound (for example, patent reference 2).

The compound of formula (B) has a 4-acetyl-phenoxy group and a pyrrolidinyl group that are a part of the constitutive elements of the compounds of the present invention, but its structure differs from

that of the compounds of the present invention in that a propylene group exists between the 4-acetyl-phenoxy group and the pyrrolidinyl group in the former. In addition, the position of the nitrogen atom in the pyrrolidinyl group in formula (B) differs from that in the compounds of the present invention.

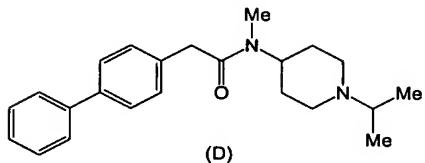
5 A compound of the following formula (C):



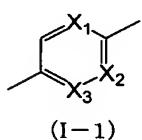
is described as a histamine-H3 receptor antagonistic compound (for example, patent reference 3).

The compound of formula (C) has an octahydropyrido[1,2-a]pyrazinyl group, but this differs from the compounds of the present invention in that the moiety Y in a formula (I) representing the latter is 10 a monocyclic or bicyclic group having one nitrogen atom in the ring, such as a pyrrolidinyl group or an octahydroquinolindinyl group. In addition, they essentially differ in the point of their structures in that, in formula (C), the octahydropyrido[1,2-a]pyrazinyl group bonds to the oxygen atom via a propylene group therebetween, but in the compounds of the present invention, the corresponding groups bond directly to each other with no alkylene group therebetween.

15 A compound having an N-isopropyl-piperidin-4-yl group of the following formula (D):

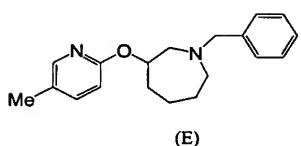


is described as a compound that strongly and selectively bind to a histamine-H3 receptor (for example, patent reference 4). The compound of formula (D) corresponds to the compounds of the present invention in that it has an N-isopropylpiperidin-4-yl group, but they differ in the following points: The 20 compounds of formula (I) of the present invention do not have a biphenyl group; and in the compound of formula (D), the biphenyl group bonds to the N-isopropylpiperidin-4-yl group via a carbamoylmethyl group therebetween, but in the compounds of formula (I) of the present invention, the substituted piperidinyl group bonds to a group of formula (I-1):



25 wherein the symbols have the same meanings as above, via an oxygen atom therebetween.

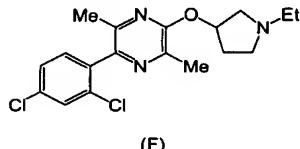
A compound having an N-benzylhomopiperidin-3-yloxy group of the following formula (E):



is described (for example, patent reference 5).

The compound of formula (E) differs from the compounds of the present invention in the point of the position of N of homopiperidine. Further, the compound of formula (E) has the property of a nicotinic acetylcholine receptor ligand, but the compounds of the present invention have the property of a histamine-H3 receptor antagonist or inverse-agonist. In addition, patent reference 5 does neither have a description to say that the compound of formula (E) may act as a histamine-H3 receptor antagonist or inverse-agonist, nor have a description to suggest it.

5 A compound having an N-ethylpyrrolidin-3-yloxyphrazinyl group of the following formula (F):



10 is described (for example, patent reference 6). The structure of the compound of formula (F) differs from that of the compounds of the present invention in that the former has a methyl group at the 3- and 6-positions of the pyrazine ring in formula (F). Regarding its use, the compound of formula (F) is a CRF receptor ligand, and patent reference 6 does neither have a description to say that the compound may act as a histamine-H3 receptor antagonist or inverse-agonist, nor have a description to suggest it.

15 patent reference 1 WO02/40461

patent reference 2 WO02/06223

patent reference 3 JP-A 2003-064081

patent reference 4 WO03/024929

patent reference 5 WO01/19817

20 patent reference 6 WO01/60806

non patent reference 1 *Life Science*, Vol. 17, 1975, p. 503)

non patent reference 2 *Journal of Comprehensive Neurology*, Vol. 273, p. 283)

non patent reference 3 *Progress in Neurobiology*, Vol. 63, p. 637 (2001)

non patent reference 4 *Trends in Pharmacological Science*, Vol. 8, p. 24 (1986)

25 non patent reference 5 *Molecular Pharmacology*, Vol. 55, p. 1101 (1999)

non patent reference 6 *Trends in Pharmacological Science*, Vol. 19, p. 177 (1998)

non patent reference 7 *Nature*, Vol. 408, p. 860)

non patent reference 8 *Brain Research*, Vol. 523, p. 325 (1990)

non patent reference 9 *Life Science*, Vol. 48, p. 2397 (1991)

30 non patent reference 10 *Brain Research*, Vol. 793, p. 279 (1998)

non patent reference 11 *Life Science*, Vol. 69, p. 469 (2001)

non patent reference 12 *Journal of Physiology and Pharmacology*, Vol. 49, p. 191 (1998)

non patent reference 13 *Behavioural Brain Research*, Vol. 104, p. 147 (1999)

non patent reference 14 *Pharmacology Biochemistry and Behavior*, Vol. 68, p. 735 (2001)

35 non patent reference 15 *European Journal of Pharmacology*, Vol. 234, p. 129 (1993)

[Problems that the Invention is to Solve]

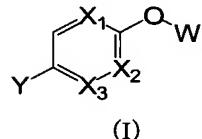
The present invention is to provide a heteroaryloxy-nitrogen-containing saturated heterocyclic derivative that has an action of antagonizing histamine to bond to a histamine-H3 receptor, or has an activity of inhibiting the homeostatic activity of a histamine-H3 receptor, and to provide a preventive or a remedy comprising it for metabolic system diseases such as obesity, diabetes, hormone secretion disorder, hyperlipemia, gout, fatty liver; circulatory system diseases, for example, stenocardia, acute/congestive cardiac insufficiency, cardiac infarction, coronary arteriosclerosis, hypertension, nephropathy, and central and peripheral nervous system diseases such as bulimia, emotional disorder, melancholia, anxiety, epilepsy, delirium, dementia, schizophrenia, attention deficit/hyperactivity disorder, memory disorder, Alzheimer's disease, Parkinson's disease, sleep disorder, recognition disorder, motion disorder, paresthesia, dysosmia, epilepsy, morphine resistance, narcotic dependency, alcoholic dependency.

[Means for Solving the Problems]

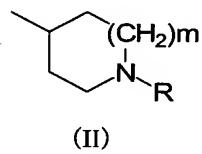
We, the present inventors have assiduously studied for the purpose of developing a compound that prevents histamine from binding to a histamine-H3 receptor and, as a result, have found that the compounds of the invention, heteroaryloxy-cycloalkylamine derivatives characterized by having an action as a histamine-H3 receptor antagonist and/or inverse-agonist are novel substances not described in publications, and have found that specific compounds including the compounds are effective as a histamine-H3 receptor antagonist or inverse-agonist. On the basis of these findings, we have completed the present invention.

Specifically, the invention relates to the following:

(1) A compound of the following formula (I) or its pharmaceutically-acceptable salt:



[wherein X^1 , X^2 and X^3 each independently represent N or CH (provided that all of X^1 , X^2 and X^3 are not CH at the same time); W represents a group of the following formula (II):



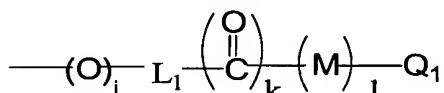
(wherein m indicates an integer of from 0 to 3; R represents a linear or branched lower alkyl group (excepting a methyl group), a cycloalkyl group having from 3 to 9 carbon atoms, an aralkyl group or a heterocyclic group having from 3 to 8 carbon atoms (the hetero ring has 1 or 2 nitrogen atoms or oxygen atoms), which may be substituted with a group selected from a class consisting of a cyano group, a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxyl group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower alkylsulfonyl group, a cyclo-lower alkylsulfonyl group, a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a cycloalkyliminocarbonyl

group and a trifluoromethyl group), or represents a group of a formula (III):



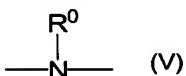
(III)

(wherein m_1 indicates an integer of from 0 to 3; n indicates an integer of from 0 to 2); Y represents a group of a formula (IV):



(IV)

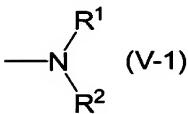
(wherein j , k and l each independently indicate 0 or 1; L_1 represents a lower alkylene group having from 1 to 4 carbon atoms, or a single bond; M represents an oxygen atom or a group of a formula (V):



(V)

(wherein R^0 represents a lower alkyl group having from 1 to 4 carbon atoms); Q_1 represents a linear or

10 branched lower alkyl group, a cycloalkyl group having from 3 to 9 carbon atoms, a phenyl group, a 5-membered or 6-membered heteroaryl group, a heterocyclic group having from 3 to 8 carbon atoms (the hetero ring may have from 1 to 3 nitrogen atoms or oxygen atoms), a naphthyl group or a condensed-cyclic heteroaryl group, which may be substituted with a group selected from a class consisting of a cyano group, a hydroxy group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower alkylsulfonyl group, a cyclo-lower 15 alkylsulfonyl group, a halogen atom, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a trifluoromethyl group, a mono-lower alkylamino group, a di-lower alkylamino group, an alkanoyl group, an alkoxy carbonylamino 20 group (the nitrogen atom in the group may be substituted with a lower alkyl group), an alkanoylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group) and an alkylsulfonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), or represents a group of a formula (V-1):



(V-1)

25 (wherein R^1 and R^2 are the same or different, each representing a lower alkyl group or a mono- or di-lower alkylcarbamoyl group, or R^1 and R^2 together form, along with the adjacent nitrogen atom, a 3- to 9-membered lactam ring, a heterocyclic group having from 3 to 8 carbon atoms (the group has 1 or 2 nitrogen atoms or oxygen atoms as the constitutive atoms thereof), a 5-membered heteroaryl group, or a condensed-cyclic heteroaryl group)].

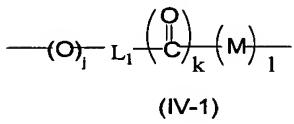
(2) The compound of above (1), wherein R in formula (II) is a cycloalkyl group having from 3 to 9 carbon atoms or a heterocyclic group having from 3 to 8 carbon atoms (the hetero ring has 1 or 2 nitrogen atoms or oxygen atoms), which may be substituted with a group selected from a class consisting of a cyano group, a hydroxy group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group, a mono-lower alkylaminocarbonyloxy group and a di-lower alkylaminocarbonyloxy group, or a represents a group of a formula (III):



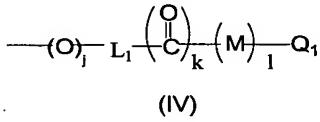
(III)

(wherein the symbols have the same meanings as above).

10 (3) The compound of above (1) or (2), wherein the group of formula (IV-1):



(wherein the symbols have the same meanings as above) in the formula (IV):

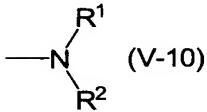
(wherein the symbols have the same meanings as above) is a C_{1-4} lower alkylene group, a carbonyl group,

15 $-\text{C}(\text{O})\text{---O}$ -, a $-\text{C}_{1-4}$ lower alkylene- $\text{C}(\text{O})$ -, a $-\text{C}_{1-4}$ lower alkylene- $\text{C}(\text{O})\text{---O}$ -, a $-\text{C}_{1-4}$ lower alkylene- $\text{C}(\text{O})\text{---N}(\text{R}^0)$ -, $-\text{C}(\text{O})\text{---N}(\text{R}^0)$ -, $-\text{O}\text{---C}_{1-4}$ lower alkylene-, or a single bond.

20 (4) The compound of above (3), wherein Q_1 is a linear or branched lower alkyl group, a cycloalkyl group having from 3 to 9 carbon atoms, a phenyl group or a naphthyl group, which may be substituted with a group selected from a class consisting of a cyano group, a hydroxy group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower alkylsulfonyl group, a cyclo-lower alkylsulfonyl group, a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a trifluoromethyl group, a mono-lower alkylamino group, a di-lower alkylamino group, an alkanoyl group, an alkoxy carbonyl amino group (the nitrogen atom in the group may be substituted with a lower alkyl group), an alkanoyl amino group (the nitrogen atom in the group may be substituted with a lower alkyl group) and an alkylsulfonyl amino group (the nitrogen atom in the group may be substituted with a lower alkyl group), or represents a 5- or 6-membered heteroaryl group having from 1 to 3 hetero atoms selected from a group consisting of an oxygen atom, a sulfur atom and a nitrogen atom, a heterocyclic group having from 3 to 8 carbon atoms and having from 1 to 3 nitrogen atoms or oxygen atoms in the

ring, or a mono- to tri-cyclic condensed-cyclic heteroaryl group optionally having from 1 to 3 hetero atoms selected from a group consisting of an oxygen atom, a sulfur atom and a nitrogen atom in each ring.

(5) The compound of above (3), wherein Q₁ of the formula (V-1) is a group of a formula (V-10):



(wherein R¹⁰ and R²⁰ together form, along with the adjacent nitrogen atom, a 3- to 9-membered lactam ring, a heterocyclic ring having from 3 to 8 carbon atoms (R¹⁰ and R²⁰ may have, apart from the adjacent nitrogen atom, 1 or 2 nitrogen atoms or oxygen atoms in the ring as the constitutive atoms of the hetero ring), a 5-membered heteroaryl group having from 1 to 4 nitrogen atoms in the ring, or a bicyclic condensed-cyclic heteroaryl group having from 1 to 3 nitrogen atoms or oxygen atoms in each ring).

(6) The compound of above (1), wherein -Y in formula (I) is a phenyl group, a pyridyl group, a pyridazinyl group or a pyrimidinyl group, which may be substituted with a group selected from a class consisting of a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower alkylsulfonyl group, a cyclo-lower alkylsulfonyl group, a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a mono-lower alkylamino group, a di-lower alkylamino group, an alkanoyl group, an alkoxy carbonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), an alkanoylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group) and an alkylsulfonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group).

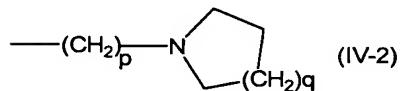
(7) The compound of above (1), wherein -Y in formula (I) is a bi- or tri-cyclic condensed ring having at least one phenyl group or pyridyl group in the ring, which may have therein 1 or 2 substituents selected from a class consisting of a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower alkylsulfonyl group, a cyclo-lower alkylsulfonyl group, a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a mono-lower alkylamino group, a di-lower alkylamino group, an alkanoyl group, an alkoxy carbonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), an alkanoylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group) and an alkylsulfonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group).

35 (8) The compound of above (1), wherein -Y in formula (I) is a furyl group, a thienyl group, a pyrrolyl group, an imidazolyl group, a pyrazolyl group, a thiazolyl group, a thiadiazolyl group, an isothiazolyl group, an oxazolyl group, an isoxazolyl group, a pyridyl group, a pyridazinyl group, a

pyrimidinyl group or a pyrazinyl group, which may have in the ring thereof, 1 or 2 substituents selected from a class consisting of a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower alkylsulfonyl group, a cyclo-lower alkylsulfonyl group, a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a mono-lower alkylamino group, a di-lower alkylamino group, an alkanoyl group, an alkoxycarbonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), an alkanoylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group) and an alkylsulfonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group).

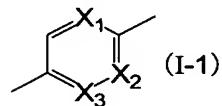
(9) The compound of above (1), wherein -Y in formula (I) is an oxetanyl group, a tetrahydrofuranyl group, a tetrahydropyranyl group, a pyrrolidinyl group, a piperidinyl group, a homopiperidinyl group, a morpholinyl group or a homomorpholinyl group, which may have in the ring thereof, 1 or 2 substituents selected from a class consisting of a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a mono-lower alkylamino group, a di-lower alkylamino group, an alkanoyl group, an alkoxycarbonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), an alkanoylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group) and an alkylsulfonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group).

25 (10) The compound of above (1), wherein -Y in the formula (I) is a group of a formula (IV-2):]



(wherein p indicates an integer of from 1 to 3; q indicates an integer of from 1 to 4).

(11) The compound of above (1) to (10), wherein at least one of X¹ and X² in the group of formula (I-1) of the formula (I):



30

(wherein the symbols have the same meanings as above) is a nitrogen atom, or both X² and X³ therein are nitrogen atoms.

(12) The compound of formula (I), which includes
2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,
35 2-(1-isopropylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,

2-(1-cyclopentylpyrrolidin-3-yloxy)-5-(4-carbamoylphenyl)pyrimidine,
 2-(1-cyclopentylpyrrolidin-3-yloxy)-5-(4-cyanophenyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{(4-methyl-1,3,5-oxadiazol-2-yl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,
 5 2-(1-cyclobutylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,
 2-(1-cyclohexylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,
 2-(1-cyclopropylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,
 2-(1-ethylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(pyrrolidin-1-ylcarbonyl)phenyl}piperidine,
 10 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(dimethylcarbamoyl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(morpholin-4-ylcarbonyl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(phenoxy)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(3-quinolinyl)piperidine,
 15 2-(1-cyclopentylpiperidin-4-yloxy)-5-{5-indolyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(pyridon-1-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(piperidon-1-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(3-quinolinyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-phenyl-4-hydroxypiperidin-1-yl)pyrimidine,
 20 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-methoxypyridin-5-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-chlorophenyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-trifluoromethylphenyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(3-pyridinyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-methoxyphenyl)pyrimidine,
 25 2-(1-cyclopentylpiperidin-4-yloxy)-5-(dibenzofuran-4-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-cyclopentyloxypyridin-5-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-pyridon-5-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(1-cyclopentyl-2-pyridon-3-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{2-(pyrrolidin-1-ylcarbonyl)pyridin-5-yl}pyrimidine,
 30 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-cyano-5-thenyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(oxomorpholin-4-yl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(2-oxazolidin-3-yl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-methyl-3-pyridin-5-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-fluoro-3-pyridin-5-yl)pyrimidine,
 35 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(2-pyridon-1-yl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(methylsulfonyl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-acetylphenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-trifluoromethoxyphenyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(2-hydroxy-2-propyl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-ethylpyridin-5-yl)pyrimidine,

2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrazine,
 5-(1-cyclopentylpiperidin-4-yloxy)-2-(4-cyanophenyl)pyridine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyridazine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(piperidin-1-ylcarbonyl)pyrimidine,

5 2-(1-cyclopentylpiperidin-4-yloxy)-5-(piperidin-1-ylmethyl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-phenylpiperazin-1-ylmethyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-cyanopyrimidin-5-yl)pyrimidine,.

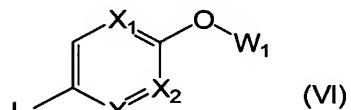
(13) A histamine-H3 receptor antagonist or inverse-agonist containing, as the active ingredient thereof, a compound of any of above (1) to (12).

10 (14) A histamine-H3 receptor antagonist containing, as the active ingredient thereof, a compound of any of above (1) to (12).

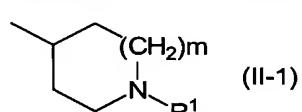
(15) A histamine-H3 receptor inverse-agonist containing, as the active ingredient thereof, a compound of any of above (1) to (12).

15 (16) A preventive or remedy comprising, as the active ingredient thereof, a compound of any of above (1) to (7), which is for metabolic system diseases such as obesity, diabetes, hormone secretion disorder, hyperlipemia, gout, fatty liver; circulatory system diseases, for example, stenocardia, acute/congestive cardiac insufficiency, cardiac infarction, coronary arteriosclerosis, hypertension, nephropathy, and central and peripheral nervous system diseases such as bulimia, emotional disorder, melancholia, anxiety, epilepsy, delirium, dementia, shinzoephrenia, attention deficit/hyperactivity disorder, 20 memory disorder, Alzheimer's disease, Parkinson's disease, sleep disorder, recognition disorder, motion disorder, paresthesia, dysosmia, epilepsy, morphine resistance, narcotic dependency, alcoholic dependency.

(17) A method for producing a compound of a general formula (I-2) or a compound of a general formula (I-3) or a salt thereof, which comprises reacting a compound of a general formula (IV):

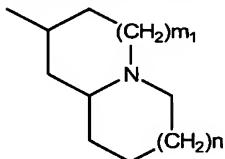


[wherein X^1 , X^2 and X^3 each independently represent N or CH (provided that all of X^1 , X^2 and X^3 are not CH at the same time); W^1 represents a group of the following formula (II-1):



(wherein m indicates an integer of from 0 to 3; R^1 represents a linear or branched lower alkyl group (excepting a methyl group), a cycloalkyl group having from 3 to 9 carbon atoms, an aralkyl group or a heterocyclic group having from 3 to 8 carbon atoms (the hetero ring has 1 or 2 nitrogen atoms or oxygen atoms), which may be substituted with a group selected from a class consisting of a cyano group, a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxyl group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower

alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a cycloalkyliminocarbonyl group and a trifluoromethyl group, or represents a group corresponding to R but having a protective group suitably introduced into the substituent which R has), or represents a group or a formula (III):

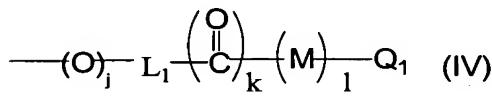


5 (III)

(wherein m_1 indicates an integer of from 0 to 3; n indicates an integer of from 0 to 2); and L3 represents a leaving group], with a compound of a general formula (XI):

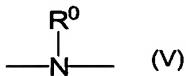
Met—Y^{1p} (XI)

[wherein Met represents a general organic metal atom; Y^{1p} represents a group of a formula (IV):

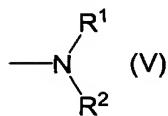


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(wherein j , k and l each independently indicate 0 or 1; L1 represents a lower alkylene group having from 1 to 4 carbon atoms, or a single bond; M represents an oxygen atom or a group of a formula (V):

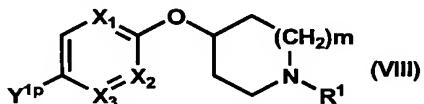


(wherein R⁰ represents a lower alkyl group having from 1 to 4 carbon atoms); Q₁ represents a linear or branched lower alkyl group, a cycloalkyl group having from 3 to 9 carbon atoms, a phenyl group, a 5-membered or 6-membered heteroaryl group, a heterocyclic group having from 3 to 8 carbon atoms (the hetero ring may have 1 or 2 nitrogen atoms or oxygen atoms), a naphthyl group or a condensed-cyclic heteroaryl group, which may be substituted with a group selected from a class consisting of a cyano group, a hydroxy group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower alkylsulfonyl group, a cyclo-lower alkylsulfonyl group, a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a trifluoromethyl group, a mono-lower alkylamino group, a di-lower alkylamino group, an alkanoyl group, an alkoxy carbonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), an alkanoylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group) and an alkylsulfonylamino group (the nitrogen atom in the group may be substituted with a lower alkyl group), or represents a group corresponding to Q¹ but having a protective group optionally introduced into the substituent which Q¹ has, or represents a group of a formula (V):

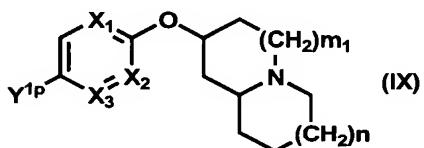


(wherein R¹ and R² are the same or different, each representing a lower alkyl group or a mono- or di-lower alkylcarbamoyl group, or R¹ and R² together form, along with the adjacent nitrogen atom, a 3- to 9-membered lactam ring, a heterocyclic group having from 3 to 8 carbon atoms (the group has 1 or 2

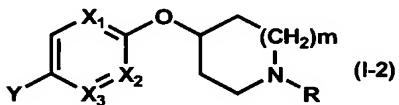
5 nitrogen atoms or oxygen atoms in the ring thereof), a 5-membered heteroaryl group or a condensed-cyclic heteroaryl group), or represents a group corresponding to -Y but having a protective group optionally introduced into the substituent which -Y has], in the presence of a catalyst, to give a compound of a general formula (VIII):



10 (wherein X¹, X², X³, m, R¹ and Y^{1p} have the same meanings as above), or a compound of a general formula (IX):

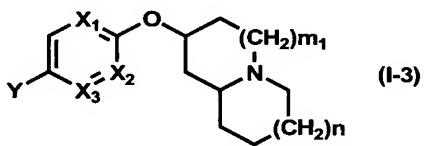


(wherein X¹, X², X³, m¹, n and Y^{1p} have the same meanings as above), and optionally removing the protective group to give a compound of a general formula (I-2):



15

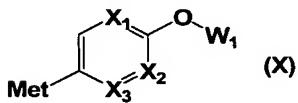
(wherein X¹, X², X³, m, R and Y have the same meanings as above), or a compound of a general formula (I-3):



(wherein X¹, X², X³, m¹, n and Y have the same meanings as above), or a salt thereof.

20

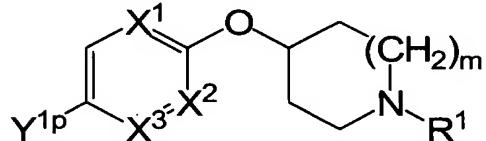
(18) A method for producing a compound of a general formula (I-2) or a compound of a general formula (I-3) or a salt thereof, which comprises reacting a compound of a general formula (X):



[wherein the symbols have the same meanings as above], with a compound of a general formula (XI):

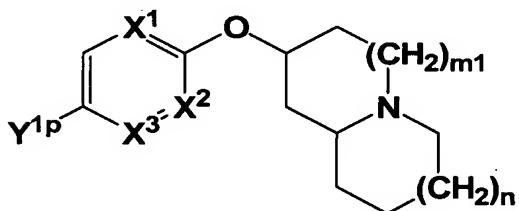


[wherein the symbols have the same meanings as above],
in the presence of a catalyst, to give a compound of a general formula (XII):



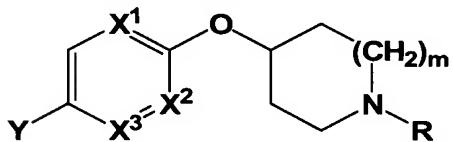
(XII)

5 (wherein X^1 , X^2 , X^3 , m , R^1 and Y^{1p} have the same meanings as above), or a compound of a general formula (XIII):



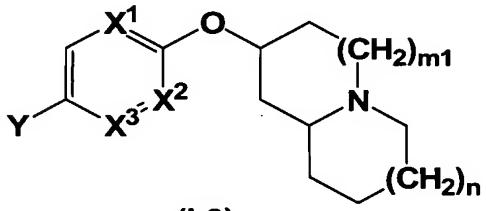
(XIII)

(wherein X^1 , X^2 , X^3 , m^1 , n and Y^{1p} have the same meanings as above), and optionally removing the protective group to give a compound of a general formula (I-2):



10 (I-2)

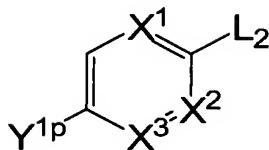
(wherein X^1 , X^2 , X^3 , m , R and Y have the same meanings as above), or a compound of a general formula (I-3):



(I-3)

(wherein X^1 , X^2 , X^3 , m^1 , n and Y have the same meanings as above), or a salt thereof.

15 (19) A method for producing a compound (I) of the invention, which comprises reacting a compound of a general formula (XIV):

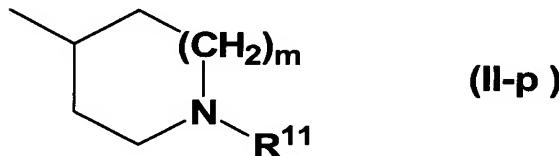


(XIV)

[wherein the symbols have the same meanings as above), with a compound of a general formula (XV):

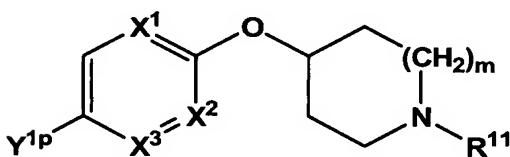


[wherein W¹ represents a group of the following formula (II-p):



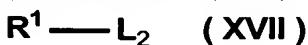
5

(wherein R¹¹ is R¹ or an amino-protective group; and the other symbols have the same meanings as above), or its salt to give a compound to give a compound of a general formula (IV-1):

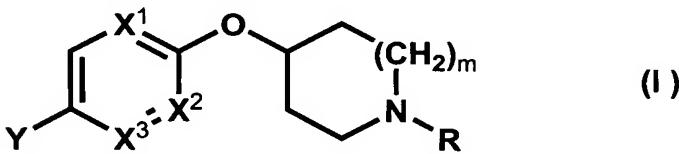


(XVI)

[wherein the symbols have the same meanings as above], and when the compound and R¹¹ have a protective group for the amino group therein, then removing the amino-protective group, and thereafter further reacting it with a precursor aldehyde or ketone corresponding to R¹ or with a compound of a general formula (XVII):



(wherein the symbols have the same meanings as above), and optionally removing the protective group to give a compound (I) of the invention:



(wherein the symbols have the same meanings as above).

The meanings of the terms used herein are mentioned below, and the compounds of the invention are described in more detail hereinunder.

20 "Aryl group" includes a hydrocarbon-cyclic aryl having from 6 to 14 carbon atoms, for example, a phenyl group, a naphthyl group, a biphenyl group, an anthryl group.

"Lower alkyl group" means a linear or branched alkyl group having from 1 to 6 carbon atoms, including, for example, a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group,

an isobutyl group, a sec-butyl group, a tert-butyl group, a pentyl group, an isoamyl group, a neopentyl group, an isopentyl group, a 1,1-dimethylpropyl group, a 1-methylbutyl group, a 2-methylbutyl group, a 1,2-dimethylpropyl group, a hexyl group, an isohexyl group, a 1-methylpentyl group, a 2-methylpentyl group, a 3-methylpentyl group, a 1,1-dimethylbutyl group, a 1,2-dimethylbutyl group, a 2,2-dimethylbutyl group, a 1,3-dimethylbutyl group, a 2,3-dimethylbutyl group, a 3,3-dimethylbutyl group, a 1-ethylbutyl group, a 2-ethylbutyl group, a 1,2,2-trimethylpropyl group, a 1-ethyl-2-methylpropyl group.

"Alkylene group" means a linear or branched alkylene group having from 1 to 6 carbon atoms, including, for example, a methylene group, an ethylene group, a trimethylene group, a tetramethylene group, a pentamethylene group.

"Cycloalkyl group having from 3 to 9 carbon atoms" includes, for example, a cyclopropyl group, a cyclobutyl group, a cyclopentyl group, a cyclohexyl group, a cycloheptyl group, a cyclooctyl group, a cyclononyl group.

"Alkoxy group" means a hydroxyl group of which the hydrogen atom is substituted with the above-mentioned lower alkyl group, including, for example, a methoxy group, an ethoxy group, a propoxy group, an isopropoxy group, a butoxy group, a sec-butoxy group, a tert-butoxy group, a pentyloxy group, an isopentyloxy group, a hexyloxy group, an isohexyloxy group.

"Alkylsulfonyl group" means a group comprising a sulfonyl group bonding to the above-mentioned alkyl group, including, for example, a methylsulfonyl group, an ethylsulfonyl group, a propylsulfonyl group, an isopropylsulfonyl group, a butylsulfonyl group.

"Alkylsulfonylamino group" means an amino group of which one hydrogen atom is substituted with the above-mentioned alkylsulfonyl group, including, for example, a methylsulfonylamino group, an ethylsulfonylamino group, a propylsulfonylamino group, an isopropylsulfonylamino group, a butylsulfonylamino group, a sec-butylsulfonylamino group, a tert-butylsulfonylamino group, an N-methyl-methylsulfonylamino group, an N-methyl-ethylsulfonylamino group, an N-methyl-propylsulfonylamino group, an N-methyl-isopropylsulfonylamino group, an N-methyl-butylsulfonylamino group, an N-methyl-sec-butylsulfonylamino group, an N-methyl-tert-butylsulfonylamino group, an N-ethyl-methylsulfonylamino group, an N-ethyl-ethylsulfonylamino group, an N-ethyl-propylsulfonylamino group, an N-ethyl-isopropylsulfonylamino group, an N-ethyl-butylsulfonylamino group, an N-ethyl-sec-butylsulfonylamino group, an N-ethyl-tert-butylsulfonylamino group.

"Cyclo-lower alkylsulfonyl group" means a group comprising a sulfonyl group bonding to the above-mentioned "cycloalkyl group having from 3 to 9 carbon atoms", including, for example, a cyclopropylsulfonyl group, a cyclobutylsulfonyl group, a cyclopentylsulfonyl group, a cyclohexylsulfonyl group, a cycloheptylsulfonyl group, a cyclooctylsulfonyl group, a cyclononylsulfonyl group.

"Aralkyl group" means the above-mentioned alkyl group having the above-mentioned aryl group, including, for example, a benzyl group, a 1-phenylethyl group, a 2-phenylethyl group, a 1-naphthylmethyl group, a 2-naphthylmethyl group.

"Hetero-aryl group" means a 5- to 7-membered monocyclic group having therein from 1 to 3

hetero atoms selected from a group consisting of an oxygen atom, a sulfur atom and a nitrogen atom, or a bicyclic hetero-aryl group comprising the mono-cyclic heteroaryl group condensed with a benzene ring or a pyridine ring, including, for example, a furyl group, a thienyl group, a pyrrolyl group, an imidazolyl group, a triazolyl group, a thiazolyl group, a thiadiazolyl group, an isothiazolyl group, an oxazolyl group, 5 an isoxazolyl group, a pyridyl group, a pyrimidinyl group, a pyridazinyl group, a pyrazolyl group, a pyrazinyl group, a quinolyl group, an isoquinolyl group, a quinazolyl group, a quinolidinyl group, a quinoxalinyl group, a cinnolinyl group, a benzimidazolyl group, an imidazopyridyl group, a triazolopyridine group, a benzofuranyl group, a naphthyridinyl group, a 1,2-benzisoxazolyl group, a benzoxazolyl group, a benzothiazolyl group, an oxazolopyridyl group, a pyridothiazolyl group, an 10 isothiazolopyridyl group, a benzothienyl group.

"Halogen atom" means, for example, a fluorine atom, a chlorine atom, a bromine atom, an iodine atom.

"Alkoxy carbonylamino group" means an amino group of which one hydrogen atom is substituted with the above-mentioned alkoxy carbonyl group, including, for example, a 15 methoxy carbonylamino group, an ethoxy carbonylamino group, a propoxycarbonylamino group, an isopropoxycarbonylamino group, a butoxycarbonylamino group, a sec-butoxycarbonylamino group, a tert-butoxycarbonylamino group, a pentyloxycarbonylamino group, an (N-methyl)methoxycarbonylamino group, an (N-methyl)ethoxycarbonylamino group, an (N-methyl)propoxycarbonylamino group, an (N-methyl)isopropoxycarbonylamino group, an (N-methyl)butoxycarbonylamino group, an 20 (N-methyl)-sec-butoxycarbonylamino group, an (N-methyl)-tert-butoxycarbonylamino group, an (N-ethyl)methoxycarbonylamino group, an (N-ethyl)ethoxycarbonylamino group, an (N-ethyl)propoxycarbonylamino group, an (N-ethyl)isopropoxycarbonylamino group, an (N-ethyl)butoxycarbonylamino group, an (N-ethyl)-sec-butoxycarbonylamino group, an (N-ethyl)-tert-butoxycarbonylamino group.

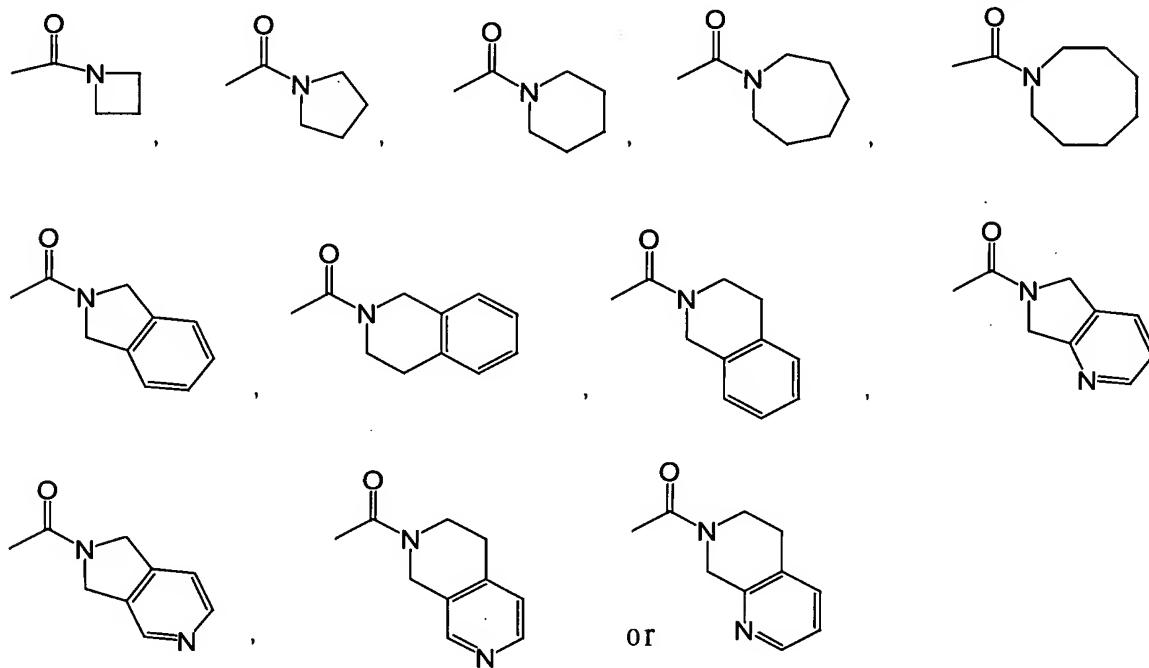
25 "Hydroxyalkyl group" means a group derived from the above-mentioned alkyl group by substituting one hydrogen atom thereof with a hydroxyl group, including, for example, a hydroxymethyl group, a hydroxyethyl group, a 1-hydroxypropyl group, a 1-hydroxyethyl group, a 2-hydroxypropyl group, a 2-hydroxy-1-methylethyl group.

30 "Mono-lower alkylcarbamoyl group" means a carbamoyl group mono-substituted with the above-mentioned lower alkyl group, including, for example, a methylcarbamoyl group, an ethylcarbamoyl group, a propylcarbamoyl group, an isopropylcarbamoyl group, a butylcarbamoyl group, a sec-butylcarbamoyl group, a tert-butylcarbamoyl group.

35 "Di-lower alkylcarbamoyl group" means a carbamoyl group di-substituted with the above-mentioned, same or different lower alkyl groups, and the "di-lower alkylcarbamoyl group" includes, for example, a dimethylcarbamoyl group, a diethylcarbamoyl group, an ethylmethylcarbamoyl group, a dipropylcarbamoyl group, a methylpropylcarbamoyl group, a diisopropylcarbamoyl group.

"Di-lower alkylcarbamoyl group" includes a 5- to 8-membered monocyclic group formed by the nitrogen atom constituting the carbamoyl group and the same or different lower alkyl groups bonding to the nitrogen atom, or includes a bicyclic group comprising the monocyclic group and a benzene ring or a

pyridine ring bonding thereto. Concretely, for example, it includes the following groups:



"Alkylamino group" means an amino group mono-substituted with the above-mentioned lower alkyl group, including, for example, a methylamino group, an ethylamino group, a propylamino group, an isopropylamino group, a butylamino group, a sec-butylamino group, a tert-butylamino group.

"Dialkylamino group" means an amino group di-substituted with the above-mentioned, same or different lower alkyl groups, including, for example, a dimethylamino group, a diethylamino group, a dipropylamino group, a methylpropylamino group, a diisopropylamino group.

"Aminoalkyl group" means a group derived from the above-mentioned alkyl group by substituting one hydrogen atom constituting it with an amino group, including, for example, an aminomethyl group, an aminoethyl group, an aminopropyl group.

"Alkanoyl group" means a group comprising a carbonyl group bonding to the above-mentioned alkyl group, including, for example, a methylcarbonyl group, an ethylcarbonyl group, a propylcarbonyl group, an isopropylcarbonyl group.

"Alkanoylamino group" means or a group comprising an amino group bonding to the above-mentioned alkanoyl group, including, for example, an acetylamino group, a propanoylamino group, a butanoylamino group, a pentanoylamino group, an N-methyl-acetylamino group, an N-methyl-propanoylamino group, an N-methyl-butanoylamino group, an N-methyl-pantanoylamino group, an N-ethyl-acetylamino group, an N-ethyl-propanoylamino group, an N-ethyl-butanoylamino group, an N-ethyl-pantanoylamino group.

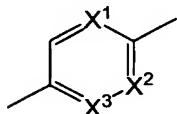
"Mono-lower alkylaminocarbonyloxy group" means a carbonyloxy group mono-substituted with the above-mentioned lower alkyl group, including, for example, a methylaminocarbonyloxy group, an ethylaminocarbonyloxy group, a propylaminocarbonyloxy group, an isopropylaminocarbonyloxy group.

"Di-lower alkylaminocarbonyloxy group" means a carbonyloxy group di-substituted with the above-mentioned lower alkyl group, including, for example, a dimethylaminocarbonyloxy group, a

diethylaminocarbonyloxy group, a diisopropylaminocarbonyloxy group, an ethylmethylaminocarbonyloxy group.

For more concretely disclosing the compounds of formula (I) of the invention, various symbols used in formula (I) are mentioned below with reference to their specific examples.

5 Group of formula (I-1):

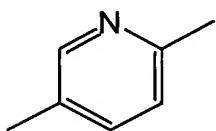


(I-1)

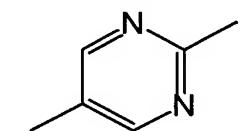
[wherein X¹, X² and X³ each independently represent N or CH (provided that all of X¹, X² and X³ are not CH at the same time)].

10 Of X¹, X² and X³, it is desirable that at least one of X¹ or X² is a nitrogen atom or both X² and X³ are nitrogen atoms.

Accordingly, preferred examples of formula (I-1) are more concretely as follows:

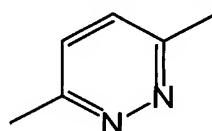


(I-10)



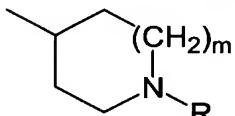
(I-11)

or



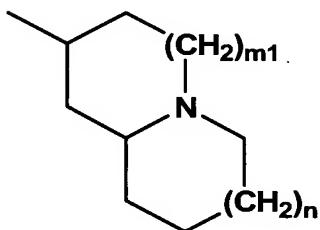
(I-12)

W in formula (I) means a group of a formula (II):



(II)

15 [wherein the symbols have the same meanings as above], or a group of a formula (III):



(III)

[wherein the symbols have the same meanings as above].

m in formula (II) is an integer of from 0 to 3.

20 R in formula (II) is a linear or branched lower alkyl group (excepting a methyl group), a cycloalkyl group having from 3 to 9 carbon atoms, an aralkyl group or a heterocyclic group having from 3 to 8 carbon atoms (the ring has 1 or 2 nitrogen atoms or oxygen atoms), which may be substituted with a group selected from a class consisting of a cyano group, a hydroxyl group, a lower alkyl group (the lower

alkyl group may be substituted with a hydroxyl group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a cycloalkyliminocarbonyl group and a trifluoromethyl group.

5 "Linear or branched lower alkyl group" represented by R in formula (II) has the same meaning as the above-defined lower alkyl group (excepting a methyl group), and includes, for example, an ethyl group, a propyl group, a butyl group, an isopropyl group, an isobutyl group, a tert-butyl group, a pentyl group, an isoamyl group, a neopentyl group, a 1,1-dimethylpropyl group, a 1-methylbutyl group, a 10 2-methylbutyl group, a hexyl group, an isohexyl group, a 1-methylpentyl group, a 1,1-dimethylbutyl group. Of these, preferred are a propyl group, a butyl group, an isopropyl group, an isobutyl group, a tert-butyl group, a pentyl group, an isoamyl group, a neopentyl group, a 1,1-dimethylpropyl group, a 15 1-methylbutyl group, a hexyl group and an isohexyl group; and of those, more preferred are an isopropyl group, an isobutyl group, a tert-butyl group, a pentyl group, an isoamyl group, a neopentyl group, a 1,1-dimethylpropyl group and a 1-methylbutyl group.

When R is a "linear or branched lower alkyl group", then the substituent that the lower alkyl group may have is preferably a cyano group, a hydroxyl group, a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a di-lower alkylaminocarbonyloxy group, a di-lower alkylcarbamoyl group or a trifluoromethyl group of the substituents mentioned above, and 20 more preferably a hydroxyl group, a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom) or a trifluoromethyl group.

25 "Lower alkyl group substituted with a cyano group" represented by R includes more concretely, for example, a 1-cyanoethyl group, a 2-cyanoethyl group, a 2-cyano-1,1-dimethyl-ethyl group, a 5-cyanopentyl group, a 4-cyanopentyl group, a 3-cyanopentyl group, a 2-cyanopentyl group, a 2-cyanopentyl group, a 1-cyanopentyl group, a 3-cyano-1-methylpropyl group, a 2-cyano-1-methylethyl group, a 1-cyanomethylpropyl group.

30 "Lower alkyl group substituted with a hydroxy group" represented by R includes more concretely, for example, a 1-hydroxyethyl group, a 2-hydroxyethyl group, a 1-hydroxypropyl group, a 2-hydroxypropyl group, a 5-hydroxypentyl group, a 4-hydroxypentyl group, a 3-hydroxypentyl group, a 2-hydroxypentyl group, a 1-hydroxypentyl group, a 1-hydroxyethyl group, a 2-hydroxyethyl group, a 2-hydroxy-1-methylethyl group, a 2-hydroxy-1-methylethyl group, a 3-hydroxy-1-methylpropyl group, a 1-hydroxymethylpropyl group, a 1,1-dimethyl-2-hydroxyethyl group.

35 "Lower alkyl group substituted with an alkoxy group (the alkoxy group may be substituted with a halogen atom)" represented by R includes more concretely, for example, a 2-(2-chloroethoxy)ethyl group, a 2-(chloromethoxy)ethyl group, a 1-methoxyethyl group, a 2-methoxyethyl group, a 2-methoxy-1-methylethyl group, a 2-chloromethoxy-1-methylethyl group, a 3-methoxy-1-methylpropyl group, a 1-(methoxymethyl)propyl group, a 3-(chloromethoxy)-1-methylpropyl group, a 1-(chloromethoxymethyl)propyl group, a 1,1-dimethyl-2-methoxyethyl group, a 2-(chloromethoxy)-1,1-dimethylethyl group, a 5-methoxypentyl group, a 4-methoxypentyl group, a

3-methoxypentyl group, a 2-methoxypentyl group, a 1-methoxypentyl group.

"Lower alkyl group substituted with a halogen atom" represented by R includes more concretely, for example, a 1-fluoroethyl group, a 2-fluoroethyl group, a 2-fluoro-1-methylethyl group, a 3-fluoro-1-methylpropyl group, a 2,2-difluoroethyl group, a 2,2,2-trifluoroethyl group, a 5 1-fluoromethylpropyl group, a 3,3-difluoropropyl group, a 3,3,3-trifluoropropyl group, a 2-fluoro-1,1-dimethylethyl group, a 1-chloroethyl group, a 2-chloroethyl group, a 2-chloro-1-methylethyl group, a 3-chloro-1-methylpropyl group, a 1-chloromethylpropyl group, a 2-chloro-1,1-dimethylethyl group.

10 "Lower alkyl group substituted with a mono-lower alkylaminocarbonyloxy group" represented by R includes more concretely, for example, a 2-(ethylaminocarbonyloxy)ethyl group, a 2-(propylaminocarbonyloxy)ethyl group, a 2-(isopropylaminocarbonyloxy)ethyl group.

15 "Lower alkyl group substituted with a dialkylaminocarbonyloxy group" represented by R includes more concretely, for example, a 1-(dimethylaminocarbonyloxy)ethyl group, a 2-(dimethylaminocarbonyloxy)ethyl group, a 1-(diethylaminocarbonyloxy)ethyl group, a 2-(diethylaminocarbonyloxy)ethyl group, a 1-(diisopropylaminocarbonyloxy)ethyl group, a 2-(dimethylaminocarbonyloxy)-1-methyl-ethyl group, a 2-(diethylcarbonyloxy)-1-methylethyl group, a 2-(diisopropylaminocarbonyloxy)-1-methylethyl group.

20 "Lower alkyl group substituted with a dialkylcarbamoyl group" represented by R includes more concretely, for example, a 2-(methylcarbamoyl)ethyl group, a 1-(methylcarbamoyl)ethyl group.

25 "Lower alkyl group substituted with a carbamoyl group" represented by R includes more concretely, for example, a 2-carbamoylethyl group, a 3-carbamoylethyl group, a 2-carbamoyl-1-methylethyl group.

30 "Lower alkyl group substituted with a trifluoromethyl group" represented by R includes more concretely, for example, a 3,3,3-trifluoropropyl group, a 2,2,2-trifluoro-1-methylethyl group, a 4,4,4-trifluorobutyl group, a 3,3,3-trifluoro-1-methylpropyl group.

"Lower alkyl group substituted with a lower alkylsulfonyl group" represented by R includes more concretely, for example, a 2-methanesulfonylethyl group, a 1-methanesulfonylethyl group, a 2-ethanesulfonylethyl group, a 2-methanesulfonyl-1-methylethyl group.

35 "Lower alkyl group substituted with a cyclo-lower alkylsulfonyl group" represented by R includes more concretely, for example, a 2-cyclopropanesulfonylethyl group, a 1-cyclopropanesulfonylethyl group, a 3-cyclobutanesulfonylpropyl group, a 2-cyclobutanesulfonylpropyl group.

"Cycloalkyl group having from 3 to 9 carbon atoms" for R is described below.

35 "Cycloalkyl group having from 3 to 9 carbon atoms" represented by R in formula (II) has the same meaning as defined hereinabove, including, for example, a cyclopropyl group, a cyclobutyl group, a cyclopentyl group, a cyclohexyl group, a cycloheptyl group, a cyclooctyl group. Of those, preferred are a cyclopropyl group, a cyclobutyl group, a cyclopentyl group and a cyclohexyl group; and more preferred are a cyclopropyl group, a cyclobutyl group and a cyclopentyl group.

When R is a "cycloalkyl group having from 3 to 9 carbon atoms", then the substituent that the

cycloalkyl group having from 3 to 9 carbon atoms may have is preferably a cyano group, a hydroxyl group, a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower alkyl group (the alkoxy group may be substituted with a halogen atom), a halogen atom, a di-lower alkylaminocarbonyloxy group, a di-lower alkylcarbamoyl group or a trifluoromethyl group of the substituents mentioned above, and more preferably a cyano group, a hydroxyl group, a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom or a trifluoromethyl group.

The cycloalkyl group having from 3 to 9 carbon atoms may have one or two and the same or different groups of these substituents at any bondable position.

"Cycloalkyl group substituted with a lower alkyl group" represented by R includes more concretely, for example, a 1-methylcyclopropyl group, a 1-ethylcyclopropyl group, a 1-methylcyclobutyl group, a 1-ethylcyclobutyl group, a 1-methylcyclopentyl group, a 1-ethylcyclopentyl group, a 1-methylcyclohexyl group, a 1-ethylcyclohexyl group, a 1-methylcycloheptyl group, a 1-ethylcycloheptyl group, a 1-methylcyclooctyl group, a 1-ethylcyclooctyl group.

"Cycloalkyl group substituted with a cyano group" represented by R includes more concretely, for example, a 2-cyanocyclopropyl group, a 3-cyanocyclopropyl group, a 2-cyanocyclobutyl group, a 2-cyanocyclopentyl group, a 3-cyanocyclopentyl group, a 2-cyanocyclohexyl group, a 3-cyanocyclohexyl group, a 4-cyanocyclohexyl group, a 2-cyanocycloheptyl group, a 3-cyanocycloheptyl group, a 4-cyanocycloheptyl group, a 2-cyanocyclooctyl group, a 3-cyanocyclooctyl group, a 4-cyanocyclooctyl group, a 5-cyanocyclooctyl group.

"Cycloalkyl group substituted with a hydroxyl group" represented by R includes more concretely, for example, a 2-hydroxycyclopropyl group, a 3-hydroxycyclobutyl group, a 2-hydroxycyclobutyl group, a 2-hydroxycyclopentyl group, a 3-hydroxycyclopentyl group, a 2-hydroxycyclohexyl group, a 3-hydroxycyclohexyl group, a 4-hydroxycyclohexyl group, a 2-hydroxycycloheptyl group, a 3-hydroxycycloheptyl group, a 4-hydroxycycloheptyl group, a 2-hydroxycyclooctyl group, a 3-hydroxycyclooctyl group, a 4-hydroxycyclooctyl group, a 5-hydroxycyclooctyl group.

"Cycloalkyl group substituted with an alkoxy group (the alkoxy group may be substituted with a halogen atom)" represented by R includes more concretely, for example, a 2-chloromethoxycyclopropyl group, a 2-methoxycyclopropyl group, a 2-ethoxycyclopropyl group, a 2-(chloromethoxy)cyclobutyl group, a 3-methoxycyclobutyl group, a 2-(chloromethoxy)cyclopentyl group, a 2-methoxycyclopentyl group, a 3-methoxycyclopentyl group, a 2-(chloromethoxy)cyclohexyl group, a 2-methoxycyclohexyl group, a 3-methoxycyclohexyl group, a 4-methoxycyclohexyl group, a 2-(chloromethoxy)cycloheptyl group, a 2-methoxycycloheptyl group, a 3-methoxycycloheptyl group, a 4-methoxycycloheptyl group, a 2-(chloromethoxy)cyclooctyl group, a 2-methoxycyclooctyl group, a 3-methoxycyclooctyl group, a 4-methoxycyclooctyl group, a 5-methoxycyclooctyl group.

"Cycloalkyl group substituted with a halogen atom" represented by R includes more concretely, for example, a 2-fluorocyclopropyl group, a 3-fluorocyclobutyl group, a 2-fluorocyclobutyl group, a 2-fluorocyclopentyl group, a 3-fluorocyclopentyl group, a 2-fluorocyclohexyl group, a

3-fluorocyclohexyl group, a 4-fluorocyclohexyl group, a 2-fluorocyclopentyl group, a 3-fluorocycloheptyl group, a 4-fluorocycloheptyl group, a 2-fluorocyclooctyl group, a 3-fluorocyclooctyl group, a 4-fluorocyclooctyl group, a 5-fluorocyclooctyl group, a 2-chlorocyclopropyl group, a 3-chlorocyclobutyl group, a 2-chlorocyclobutyl group, a 2-chlorocyclopentyl group, a 3-chlorocyclopentyl group, a 2-chlorocyclohexyl group, a 3-chlorocyclohexyl group, a 4-chlorocyclohexyl group, a 2-chlorocycloheptyl group, a 3-chlorocycloheptyl group, a 4-chlorocycloheptyl group, a 2-chlorocyclooctyl group, a 3-chlorocyclooctyl group, a 4-chlorocyclooctyl group, a 5-chlorocyclooctyl group.

"Cycloalkyl group substituted with a mono-lower alkylaminocarbonyloxy group" represented by

10 R includes more concretely, for example, a 2-(methylcarbamoyloxy)cyclopropyl group, a 3-(methylcarbamoyloxy)cyclobutyl group, a 2-(methylcarbamoyloxy)cyclobutyl group, a 2-(methylcarbamoyloxy)cyclopentyl group, a 3-(methylcarbamoyloxy)cyclopentyl group, a 2-(methylcarbamoyloxy)cyclohexyl group, a 3-(methylcarbamoyloxy)cyclohexyl group, a 4-(methylcarbamoyloxy)cyclohexyl group, a 2-(methylcarbamoyloxy)cycloheptyl group, a 3-(methylcarbamoyloxy)cycloheptyl group, a 2-(methylcarbamoyloxy)cyclooctyl group, a 3-(methylcarbamoyloxy)cyclooctyl group, a 4-(methylcarbamoyloxy)cyclooctyl group, a 5-(methylcarbamoyloxy)cyclooctyl group.

"Cycloalkyl group substituted with a di-lower alkylaminocarbonyloxy group" represented by R includes more concretely, for example, a 2-(dimethylcarbamoyloxy)cyclopropyl group, a

20 3-(dimethylcarbamoyloxy)cyclobutyl group, a 2-(dimethylcarbamoyloxy)cyclobutyl group, a 2-(dimethylcarbamoyloxy)cyclopentyl group, a 3-(dimethylcarbamoyloxy)cyclopentyl group, a 2-(dimethylcarbamoyloxy)cyclohexyl group, a 3-(dimethylcarbamoyloxy)cyclohexyl group, a 4-(dimethylcarbamoyloxy)cyclohexyl group, a 2-(dimethylcarbamoyloxy)cycloheptyl group, a 3-(dimethylcarbamoyloxy)cycloheptyl group, a 4-(dimethylcarbamoyloxy)cycloheptyl group, a 2-(dimethylcarbamoyloxy)cyclooctyl group, a 3-(dimethylcarbamoyloxy)cyclooctyl group, a 4-(dimethylcarbamoyloxy)cyclooctyl group, a 5-(dimethylcarbamoyloxy)cyclooctyl group.

"Cycloalkyl group substituted with a dialkylcarbamoyl group" represented by R includes more concretely, for example, a 2-(dimethylcarbamoyl)cyclopropyl group, a 3-(dimethylcarbamoyl)cyclobutyl group, a 2-(dimethylcarbamoyl)cyclobutyl group, a 2-(dimethylcarbamoyl)cyclopentyl group, a

30 3-(dimethylcarbamoyl)cyclopentyl group, a 2-(dimethylcarbamoyl)cyclohexyl group, a 3-(dimethylcarbamoyl)cyclohexyl group, a 4-(dimethylcarbamoyl)cyclohexyl group, a 2-(dimethylcarbamoyl)cycloheptyl group, a 3-(dimethylcarbamoyl)cycloheptyl group, a 4-(dimethylcarbamoyl)cycloheptyl group, a 2-(dimethylcarbamoyl)cyclooctyl group, a 3-(dimethylcarbamoyl)cyclooctyl group, a 4-(dimethylcarbamoyl)cyclooctyl group, a 5-(dimethylcarbamoyl)cyclooctyl group.

"Cycloalkyl group substituted with an alkylcarbamoyl group" represented by R includes more concretely, for example, a 2-(methylcarbamoyl)cyclopropyl group, a 3-(methylcarbamoyl)cyclobutyl group, a 2-(methylcarbamoyl)cyclobutyl group, a 2-(methylcarbamoyl)cyclopentyl group, a 3-(methylcarbamoyl)cyclopentyl group, a 2-(methylcarbamoyl)cyclohexyl group, a

	3-(methylcarbamoyl)cyclohexyl	group,	a	4-(methylcarbamoyl)cyclohexyl	group,	a
	2-(methylcarbamoyl)cycloheptyl	group,	a	3-(methylcarbamoyl)cycloheptyl	group,	a
	4-(methylcarbamoyl)cycloheptyl	group,	a	2-(methylcarbamoyl)cyclooctyl	group,	a
	3-(methylcarbamoyl)cyclooctyl	group,	a	4-(methylcarbamoyl)cyclooctyl	group,	a
5	5-(methylcarbamoyl)cyclooctyl group.					

"Cycloalkyl group substituted with a carbamoyl group" represented by R includes more concretely, for example, a 2-carbamoylcyclopropyl group, a 3-carbamoylcyclobutyl group, a 2-carbamoylcyclobutyl group, a 2-carbamoylcyclopentyl group, a 3-carbamoylcyclopentyl group, a 2-carbamoylcyclohexyl group, a 3-carbamoylcyclohexyl group, a 4-carbamoylcyclohexyl group, a 2-carbamoylcycloheptyl group, a 3-carbamoylcycloheptyl group, a 4-carbamoylcycloheptyl group, a 2-carbamoylcyclooctyl group, a 3-carbamoylcyclooctyl group, a 4-carbamoylcyclooctyl group, a 5-carbamoylcyclooctyl group.

"Cycloalkyl group substituted with a trifluoromethyl group" represented by R includes more concretely, for example, a 2-(trifluoromethyl)cyclopropyl group, a 2-(trifluoromethyl)cyclobutyl group, a 3-(trifluoromethyl)cyclobutyl group, a 3-(trifluoromethyl)cyclopentyl group, a 3-(trifluoromethyl)cyclohexyl group, a 2-(trifluoromethyl)cycloheptyl group, a 4-(trifluoromethyl)cycloheptyl group, a 2-(trifluoromethyl)cyclooctyl group, a 3-(trifluoromethyl)cyclooctyl group, a 4-(trifluoromethyl)cyclooctyl group, a 5-(trifluoromethyl)cyclooctyl group.

"Cycloalkyl group substituted with a lower alkylsulfonyl group" represented by R includes more concretely, for example, a 2-methanesulfonylcyclopropyl group, a 2-methanesulfonylcyclobutyl group, a 3-methanesulfonylcyclobutyl group, a 3-methanesulfonylcyclopentyl group, a 3-methanesulfonylcyclohexyl group, a 2-methanesulfonylcycloheptyl group, a 4-methanesulfonylcycloheptyl group, a 2-methanesulfonylcyclooctyl group, a 3-methanesulfonylcyclooctyl group, a 4-methanesulfonylcyclooctyl group, a 5-methanesulfonylcyclooctyl group.

"Cycloalkyl group substituted with a cyclo-lower alkylsulfonyl group" represented by R includes more concretely, for example, a 2-cyclopropanesulfonylcyclopropyl group, a 2-cyclopropanesulfonylcyclobutyl group, a 3-cyclopropanesulfonylcyclobutyl group, a 2-cyclopropanesulfonylcyclopentyl group, a 3-cyclopropanesulfonylcyclopentyl group, a 2-cyclopropanesulfonylcyclohexyl group, a 3-cyclopropanesulfonylcyclohexyl group, a 2-cyclopropanesulfonylcycloheptyl group, a 3-cyclopropanesulfonylcycloheptyl group, a 2-cyclopropanesulfonylcyclooctyl group, a 3-cyclopropanesulfonylcyclooctyl group, a 4-cyclopropanesulfonylcyclooctyl group, a 5-cyclopropanesulfonylcyclooctyl group.

"Aralkyl group" for R is described.

"Aralkyl group" represented by R in formula (II) means an alkyl group such as that mentioned above but having a hydrocarbon-cyclic aryl group with from 6 to 14 carbon atoms such as a phenyl group, a naphthyl group or a biphenyl group, and it includes, for example, a benzyl group, a 2-phenylethyl group, a 1-phenylethyl group, a 1-naphthylmethyl group, a 2-naphthylmethyl group, a 1-naphthalene-1-ethyl group, a 1-naphthalen-2-ylethyl group. Of those, preferred are a benzyl group, a 2-phenylethyl group, a 1-phenylethyl group, a 1-naphthylmethyl group and a 2-naphthylmethyl group; and more preferred are a benzyl group, a 2-phenylethyl group, a 1-phenylethyl group and a 1-naphthylmethyl group.

When R is an "aralkyl group", then the substituent that the aralkyl group may have is preferably a cyano group, a hydroxyl group, a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a di-lower alkylaminocarbonyloxy group, a di-lower alkylcarbamoyl group or a trifluoromethyl group of the substituents mentioned above, and more preferably a cyano group, a hydroxyl group, a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom or a trifluoromethyl group.

The aralkyl group may have one or two and the same or different groups of these substituents at any bondable position.

"Aralkyl group substituted with a cyano group" represented by R includes more concretely, for example, a 4-cyanobenzyl group, a 1-(4-cyanophenyl)ethyl group, a 2-(4-cyanophenyl)ethyl group.

"Aralkyl group substituted with a hydroxyl group" represented by R includes more concretely, for example, a 4-hydroxybenzyl group, a 1-(4-hydroxyphenyl)ethyl group, a 2-(4-hydroxyphenyl)ethyl group.

"Aralkyl group substituted with an alkoxy group (the alkoxy group may be substituted with a halogen atom)" represented by R includes more concretely, for example, a 2-methoxybenzyl group, a 3-methoxybenzyl group, a 4-methoxybenzyl group, a 2-chloromethoxybenzyl group, a 2-(4-methoxyphenyl)ethyl group, a 2-(3-methoxyphenyl)ethyl group, a 2-(2-methoxyphenyl)ethyl group, a 1-(4-methoxyphenyl)ethyl group, a 1-(3-methoxyphenyl)ethyl group, a 1-(2-methoxyphenyl)ethyl group.

"Aralkyl group substituted with halogen atom" represented by R includes more concretely, for example, a 4-chlorobenzyl group, a 1-(4-chlorophenyl)ethyl group, a 2-(4-chlorophenyl)ethyl group.

"Aralkyl group substituted with an alkylaminocarbonyloxy group" represented by R includes more concretely, for example, a 4-(methylcarbamoyloxy)benzyl group, a 4-(ethylcarbamoyloxy)benzyl group, a 4-(methylcarbamoyloxy)benzyl group, a 4-(cyclopropylcarbamoyloxy)benzyl group.

"Aralkyl group substituted with a dialkylaminocarbonyloxy group" represented by R includes more concretely, for example, a 4-(dimethylaminocarbonyloxy)benzyl group, a 4-(ethylmethylcarbamoyloxy)benzyl group, a 4-(diethylcarbamoyloxy)benzyl group.

"Aralkyl group substituted with a dialkylcarbamoyl group" represented by R includes more concretely, for example, a 4-dimethylcarbamoylbenzyl group, a 4-(ethylmethylcarbamoyl)benzyl group, a 2-(3-dimethylcarbamoylphenyl)ethyl group.

"Aralkyl group substituted with an alkylcarbamoyl group" represented by R includes more

concretely, for example, a 4-(methylcarbamoyl)benzyl group, a 3-(methylcarbamoyl)benzyl group, a 2-(methylcarbamoyl)benzyl group, a 2-(3-ethylcarbamoylphenyl)ethyl group, a 2-(4-methylcarbamoylphenyl)ethyl group.

"Aralkyl group substituted with a carbamoyl group" represented by R includes more concretely, for example, a 4-carbamoylbenzyl group, a 3-carbamoylbenzyl group, a 2-carbamoylbenzyl group, a 2-(3-carbamoylphenyl)ethyl group, a 2-(4-carbamoylphenyl)ethyl group.

"Aralkyl group substituted with a trifluoromethyl group" represented by R includes more concretely, for example, a 4-(trifluoromethyl)benzyl group, a 3-(trifluoromethyl)benzyl group, a 2-(trifluoromethyl)benzyl group, a 2-(3-trifluoromethylphenyl)ethyl group, a 2-(4-trifluoromethylphenyl)ethyl group.

"Aralkyl group substituted with a lower alkylsulfonyl group" represented by R includes more concretely, for example, a 4-methanesulfonylbenzyl group, a 3-methanesulfonylbenzyl group, a 2-methanesulfonylbenzyl group, a 4-ethanesulfonylbenzyl group, a 3-ethanesulfonylbenzyl group, a 2-ethanesulfonylbenzyl group, a 2-(3-methanesulfonylphenyl)ethyl group, a 2-(3-methanesulfonylphenyl)ethyl group, 2-(4-methanesulfonylphenyl)ethyl group.

"Aralkyl group substituted with a cyclo-lower alkylsulfonyl group" represented by R includes more concretely, for example, a 4-cyclopropanemethanesulfonylbenzyl group, a 3-cyclopropanemethanesulfonylbenzyl group, a 2-cyclopropanemethanesulfonylbenzyl group, a 2-(3-cyclopropanesulfonylphenyl)ethyl group, a 2-(3-cyclopropanesulfonylphenyl)ethyl group, a 2-(4-cyclopropanesulfonylphenyl)ethyl group.

"3- to 8-membered hetero ring" for R is described below.

"3 to 8-membered heterocyclic ring" represented by R in formula (II) means a 3- to 8-membered hetero ring having 1 or 2 hetero atoms of nitrogen or oxygen atoms in the ring. When the hetero ring has 2 oxygen atoms or nitrogen atoms therein, then the hetero atoms may be the same or different.

The 3- to 8-membered heterocyclic group includes, for example, an oxetanyl group, a tetrahydrofuranyl group, a tetrahydropyranyl group, an azetidinyl group, a pyrrolidinyl group, a piperidinyl group, a homopiperidinyl group, a morpholinyl group, a homomorpholinyl group, a piperazinyl group, a homopiperazinyl group. Of those, preferred are an oxetanyl group, a tetrahydrofuranyl group, a tetrahydropyranyl group, a pyrrolidinyl group, a piperidinyl group, a homopiperidinyl group, a morpholinyl group, a homomorpholinyl group; and more preferred are an oxetanyl group, a tetrahydrofuranyl group, a tetrahydropyranyl group, a piperidinyl group, a homopiperidinyl group.

When R is a "3- to 8-membered hetero ring", then the substituent that the hetero ring may have is preferably a cyano group, a hydroxyl group, a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower alkyl group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a di-lower alkylaminocarbonyloxy group, a di-lower alkylcarbamoyl group or a trifluoromethyl group of the substituents mentioned above, and more preferably a cyano group, a hydroxyl group, a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower alkyl group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom or

a trifluoromethyl group.

The 3- to 8-membered hetero ring may have one or two and the same or different groups of these substituents at any bondable position.

5 "3- to 8-membered hetero ring substituted with a cyano group" represented by R includes more concretely, for example, a 4-cyanooxetan-2-yl group, a 4-cyanotetrahydrofuran-3-yl group, a 3-cyanopiperidin-4-yl group, a 6-cyanoazepan-4-yl group.

10 "3- to 8-membered hetero ring substituted with a lower alkyl group" represented by R includes more concretely, for example, a 2-methyl-oxetan-3-yl group, a 2-chloromethyloxetan-3-yl group, a 4-methyloxetan-2-yl group, a 5-methyltetrahydrofuran-3-yl group, a 5-chloromethyltetrahydrofuran-3-yl group, a 4-methyltetrahydrofuran-2-yl group, a 2-methyltetrahydropyran-4-yl group, a 5-methylpyrrolidin-3-yl group, a 4-methylpyrrolidin-3-yl group, a 2-methylpiperidin-4-yl group, a 3-methylpiperidin-4-yl group, a 7-methylazepan-4-yl group.

15 "3- to 8-membered hetero ring substituted with a hydroxyl group" represented by R includes more concretely, for example, a 4-hydroxyoxetan-2-yl group, a 4-hydroxytetrahydrofuran-3-yl group, a 3-hydroxypiperidin-4-yl group, a 6-hydroxyazepan-4-yl group.

20 "3- to 8-membered hetero ring substituted with a halogen atom" represented by R includes more concretely, for example, a 4-fluorooxetan-2-yl group, a 3-fluorooxetan-2-yl group, a 2-fluorooxetan-3-yl group, a 4-fluorotetrahydrofuran-3-yl group, a 3-fluoropiperidin-4-yl group, a 6-fluoroazepan-4-yl group, a 4-fluorooxetan-2-yl group, a 3-fluorooxetan-2-yl group, a 2-chlorooxetan-3-yl group, a 4-chlorotetrahydrofuran-3-yl group, a 3-chloropiperidin-4-yl group, a 6-chloroazepan-4-yl group.

25 "3- to 8-membered hetero ring substituted with an alkylaminocarbonyloxy group" represented by R includes more concretely, for example, a 4-(methylcarbamoyloxy)oxetan-2-yl group, a 3-(methylcarbamoyloxy)oxetan-2-yl group, a 2-(ethylcarbamoyloxy)oxetan-3-yl group, a 4-(methylcarbamoyloxy)tetrahydrofuran-3-yl group, a 3-(methylcarbamoyloxy)piperidin-4-yl group, a 6-(methylcarbamoyloxy)azepan-4-yl group.

30 "3- to 8-membered hetero ring substituted with a dialkylaminocarbonyloxy group" represented by R includes more concretely, for example, a 4-(dimethylcarbamoyloxy)oxetan-2-yl group, a 3-(dimethylcarbamoyloxy)oxetan-2-yl group, a 2-(diethylcarbamoyloxy)oxetan-3-yl group, a 4-(ethylcarbamoyloxy)tetrahydrofuran-3-yl group, a 3-(dimethylcarbamoyloxy)piperidin-4-yl group, a 6-(dimethylcarbamoyloxy)azepan-4-yl group.

35 "3- to 8-membered hetero ring substituted with an alkylcarbamoyl group" represented by R includes more concretely, for example, a 4-(methylcarbamoyl)oxetan-2-yl group, a 3-(methylcarbamoyl)oxetan-2-yl group, a 4-(ethylcarbamoyl)tetrahydrofuran-3-yl group, a 3-(methylcarbamoyl)piperidin-4-yl group, a 6-(dimethylcarbamoyl)azepan-4-yl group.

"3- to 8-membered hetero ring substituted with a carbamoyl group" represented by R includes more concretely, for example, a 4-carbamoyloxetan-2-yl group, a 3-carbamoyloxetan-2-yl group, a 4-carbamoyltetrahydrofuran-3-yl group, a 3-carbamoylpiperidin-4-yl group, a 6-carbamoylazepan-4-yl group.

"3- to 8-membered hetero ring substituted with a trifluoromethyl group" represented by R

includes more concretely, for example, a 4-(trifluoromethyl)oxetan-2-yl group, a 3-(trifluoromethyl)oxetan-2-yl group, a 4-(trifluoromethyl)tetrahydrofuran-3-yl group, a 3-(trifluoromethyl)piperidin-4-yl group, a 6-(trifluoromethyl)azepan-4-yl group.

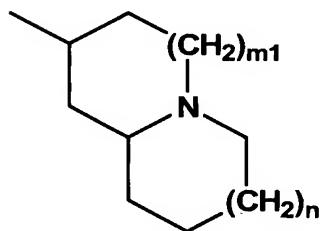
"3- to 8-membered hetero ring substituted with a lower alkylsulfonyl group" represented by R

5 includes more concretely, for example, a 4-(methylsulfonyl)oxetan-2-yl group, a 3-(ethylsulfonyl)oxetan-2-yl group, a 4-(ethylsulfonyl)tetrahydrofuran-3-yl group, a 3-(methylsulfonyl)piperidin-4-yl group, a 6-(methylsulfonyl)azepan-4-yl group.

"3- to 8-membered hetero ring substituted with a cyclo-lower alkylsulfonyl group" represented by R includes more concretely, a 4-(cyclopropylsulfonyl)oxetan-2-yl group, a

10 3-(cyclopropylsulfonyl)oxetan-2-yl group, a 4-(cyclopropylsulfonyl)tetrahydrofuran-3-yl group, a 3-(cyclopropyl)piperidin-4-yl group, a 6-(cyclopropylsulfonyl)azepan-4-yl group.

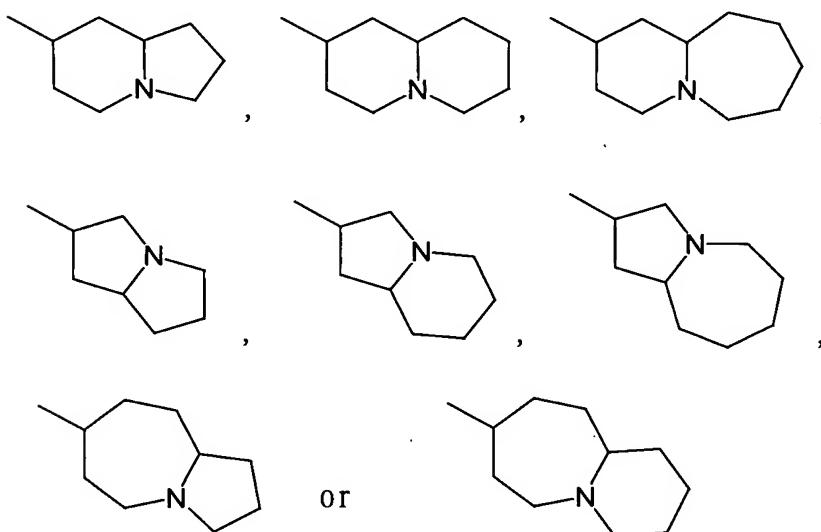
When W represents a group of a formula (III):



(III)

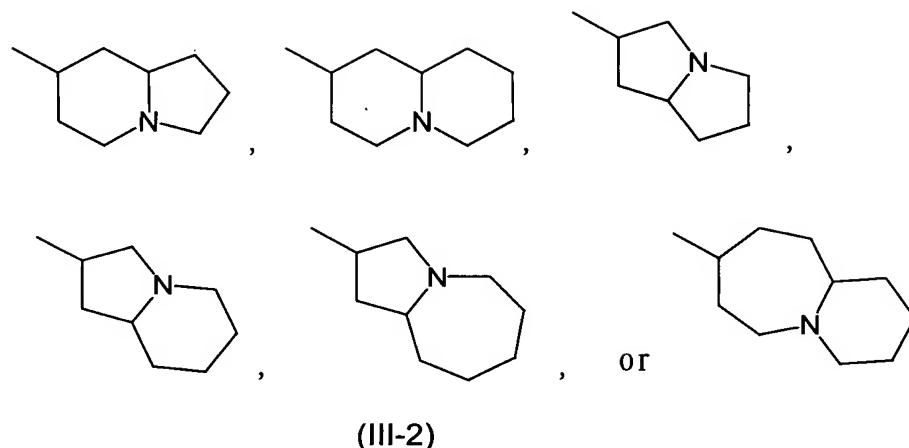
(wherein the symbols have the same meanings as above), m1 and n are independent of each other, and m indicates an integer of from 0 to 3 and n indicates an integer of from 0 to 2.

15 Specific examples of the group of formula (III) are the following formula (III-1):

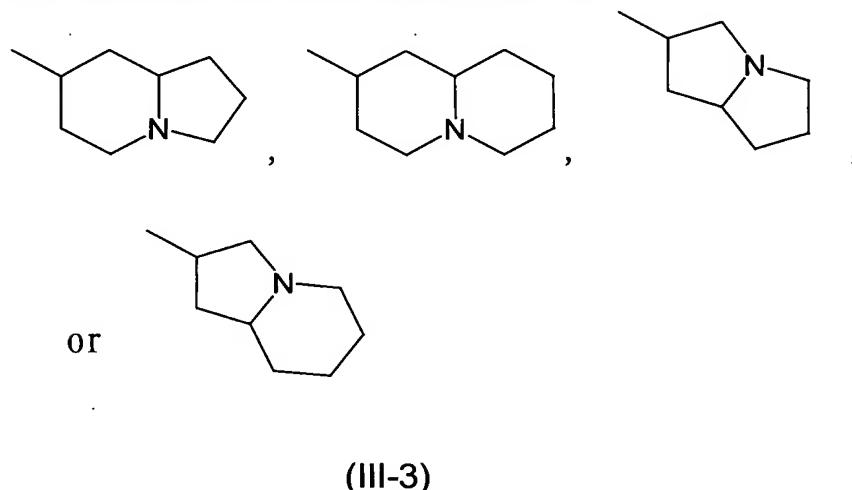


(III-1)

Of those, preferred are the following formula (III-2):



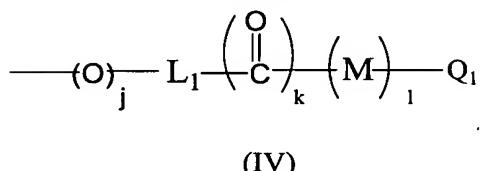
More preferred are the following formula (III-3):



5 In formula (II) or (III), when m or n in $-(CH_2)_m-$ and $-(CH_2)_n-$ is 0, then $-(CH_2)_m-$ and $-(CH_2)_n-$ mean a single bond.

Y in formula (I) is described below.

Y means a group of a formula (IV):



10 In formula (IV), j, k and l each independently indicate 0 or 1.

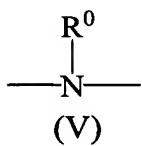
When j is 0, then $-(\text{O})_j-$ means a single bond.

When k is 0, then $-(\text{C}(\text{O}))_k-$ means a single bond.

When l is 0, then $-(\text{M})_l-$ means a single bond.

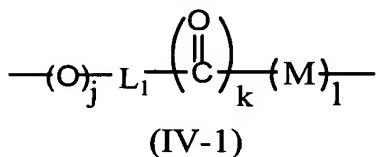
11 L₁ represents a lower alkyl group having from 1 to 4 carbon atoms, or a single bond. Of those, L₁ is preferably a lower alkyl group having from 1 to 3 carbon atoms, or a single bond, more preferably a lower alkyl group having 1 or 2 carbon atoms, or a single bond.

M represents an oxygen atom, or a group of a formula (V):



5 In formula (V), R^0 represents a lower alkyl group having from 1 to 4 carbon atoms. R^0 includes, for example, a methyl group, an ethyl group, a propyl group, an n-butyl group, an isopropyl group, an isobutyl group, a tert-butyl group. Of those, preferred are a methyl group, an ethyl group, a propyl group, an n-butyl group, an isopropyl group; and more preferred are a methyl group, an ethyl group, a propyl group, an isopropyl group.

Of the above-mentioned formula (IV), the group of the following formula (IV-1):

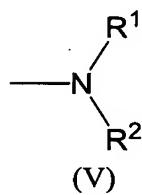


10 (wherein the symbols have the same meanings as above) is preferably a C_{1-4} lower alkylene group, a carbonyl group, $-\text{C}(\text{O})\text{---O}$, $-\text{C}_{1-4}$ lower alkylene- $\text{C}(\text{O})\text{---}$, $-\text{C}_{1-4}$ lower alkylene- $\text{C}(\text{O})\text{---O}$, $-\text{C}_{1-4}$ lower alkylene- $\text{C}(\text{O})\text{---N}(\text{R}^0)$, $-\text{C}(\text{O})\text{---N}(\text{R}^0)$, $-\text{O---C}_{1-4}$ lower alkylene-, or a single bond, more preferably a C_{1-4} lower alkylene group, $-\text{C}(\text{O})\text{---O}$, $-\text{C}_{1-4}$ lower alkylene- $\text{C}(\text{O})\text{---O}$, $-\text{C}_{1-4}$ lower alkylene- $\text{C}(\text{O})\text{---N}(\text{R}^0)$, $-\text{C}(\text{O})\text{---N}(\text{R}^0)$, $-\text{O---C}_{1-4}$ lower alkylene-, or a single bond. In these, R^0 has the same meaning as above.

15 More concretely, the group of formula (IV-1) includes, for example, a methylene group, an ethylene group, a trimethylene group, a tetramethylene group, a carbonyl group, $-\text{C}(\text{O})\text{---O}$, $-\text{CH}_2\text{---C}(\text{O})\text{---}$, $-(\text{CH}_2)_2\text{---C}(\text{O})\text{---}$, $-\text{CH}_2\text{---C}(\text{O})\text{---O}$, $-(\text{CH}_2)_2\text{---C}(\text{O})\text{---O}$, $-\text{C}(\text{O})\text{---NH}$, $-\text{C}(\text{O})\text{---N}(\text{Me})$, $-\text{CH}_2\text{---C}(\text{O})\text{---NH}$, $-\text{CH}_2\text{---C}(\text{O})\text{---N}(\text{Me})$, $-\text{O---CH}_2$, $-\text{O---(CH}_2\text{)}$, a single bond. Of those, preferred are a methylene group, an ethylene group, a carbonyl group, $-\text{C}(\text{O})\text{---O}$, $-\text{CH}_2\text{---C}(\text{O})\text{---}$, $-\text{C}(\text{O})\text{---N}(\text{Me})$, a single bond.

Q_1 is described below.

20 Q_1 represents a linear or branched lower alkyl group, a cycloalkyl group having from 3 to 9 carbon atoms, a phenyl group, a 5-membered or 6-membered heteroaryl group, a heterocyclic group having from 3 to 8 carbon atoms (the hetero ring may have from 1 to 3 nitrogen atoms or oxygen atoms), a naphthyl group or a condensed-cyclic heteroaryl group, which may be substituted with a group selected from a class consisting of a cyano group, a hydroxy group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a trifluoromethyl group, a mono-lower alkylamino group, a di-lower alkylamino group, an alkanoyl group, an alkoxy carbonyl amino group (the nitrogen atom in the group may be substituted with a lower alkyl group), an alkanoyl amino group (the nitrogen atom in the group may be substituted with a lower alkyl group) and an alkylsulfonyl amino group (the nitrogen atom in the group may be substituted with a lower alkyl group), or represents a group of a formula (V):



(wherein R¹ and R² are the same or different, each representing a lower alkyl group or a mono- or di-lower alkylcarbamoyl group, or R¹ and R² together form, along with the adjacent nitrogen atom, a 3- to 9-membered lactam ring, a heterocyclic group having from 3 to 8 carbon atoms (the group has 1 or 2 nitrogen atoms or oxygen atoms as the constitutive atoms thereof), a 5-membered heteroaryl group, or a condensed-cyclic heteroaryl group).

"Linear or branched lower alkyl group" represented by Q₁ may be the same as the lower alkyl group defined hereinabove. Of those, preferred are a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, a pentyl group, an isoamyl group, a neopentyl group, an isopentyl group, a 1,1-dimethylpropyl group, a 1-methylbutyl group, a 2-methylbutyl group, a 1,2-dimethylpropyl group, a hexyl group, an isohexyl group; and more preferred are a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, a pentyl group, an isoamyl group, a neopentyl group, an isopentyl group, a 1,1-dimethylpropyl group, a hexyl group, an isohexyl group.

-Y in which Q₁ is a "linear or branched lower alkyl group" is more concretely, for example, preferably a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, a pentyl group, an isoamyl group, a neopentyl group, a hexyl group, an isohexyl group, a heptyl group, an octyl group, a nonanyl group, a decanyl group, a methoxy group, an ethoxy group, a propoxy group, an isopropoxy group, a butoxy group, a sec-butoxy group, a tert-butoxy group, a pentyloxy group, an isoamyoxy group, a neopentyloxy group, a hexyloxy group, an isohexyloxy group, a heptyloxy group, an octyloxy group, a methoxycarbonyl group, an ethoxycarbonyl group, a propoxycarbonyl group, an isopropoxycarbonyl group, a butoxycarbonyl group, an isobutoxycarbonyl group, a sec-butoxycarbonyl group, a tert-butoxycarbonyl group, a pentyloxycarbonyl group, an isoamyoxy carbonyl group, a neopentyloxycarbonyl group, a hexyloxycarbonyl group, a methyloxycarbonylmethoxy group, an ethyloxycarbonylmethoxy group, a propyloxycarbonylmethoxy group, an isopropyloxycarbonylmethoxy group, a butyloxycarbonylmethoxy group, an isobutyloxycarbonylmethoxy group, a sec-butyloxycarbonylmethoxy group, a tert-butyloxycarbonylmethoxy group, a pentyloxycarbonylmethoxy group, an isoamyoxy carbonylmethoxy group, a neopentyloxycarbonylmethoxy group, a hexyloxycarbonylmethoxy group, a methyloxycarbonylpropoxy group, an ethyloxycarbonylpropoxy group, a propyloxycarbonylpropoxy group, an isopropyloxycarbonylpropoxy group, a butyloxycarbonylpropoxy group, an isobutyloxycarbonylpropoxy group, a sec-butyloxycarbonylpropoxy group, a tert-butyloxycarbonylpropoxy group, a pentyloxycarbonylpropoxy group, an isoamyoxy carbonylpropoxy group, a neopentyloxycarbonylpropoxy group, a hexyloxycarbonylpropoxy group; more preferably a an isopropyl group, a butyl group, a isobutyl group, a pentyl group, an isoamyl group, a neopentyl group, a hexyl group, an isohexyl group, a heptyl group, an

octyl group, a nonanyl group, a decanyl group, an isopropoxy group, a butoxy group, a sec-butoxy group, a tert-butoxy group, a pentyloxy group, an isoamyloxy group, a neopentyloxy group, a hexyloxy group, an isohexyloxy group, a heptyloxy group, an octyloxy group.

When Q_1 is a "linear or branched alkyl group", the substituent which the alkyl group may have is preferably any of a cyano group, a hydroxyl group, a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a di-lower alkylaminocarbonyloxy group, a di-lower alkylcarbamoyl group and a trifluoromethyl group of the substituents which Q_1 may have; more preferably a hydroxyl group, a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom) or a trifluoromethyl group.

-Y in which Q_1 is a "linear or branched lower alkyl group substituted with a cyano group" includes more concretely, for example, a 3-cyanopropyl group, a 4-cyanobutyl group, a 2-cyanobutyl group, a 5-cyanopentyl group, a 4-cyanopentyl group, a 6-cyanohexyl group, a 5-cyanohexyl group, a 4-cyanohexyl group, a 7-cyanoheptyl group, a 6-cyanoheptyl group, a 5-cyanoheptyl group, a 8-cyanoctyl group, a 7-cyanoctyl group, a 6-cyanoctyl group, a 5-cyanoctyl group, a 3-cyanopropoxy group, a 4-cyanobutoxy group, a 3-cyanobutoxy group, a 5-cyanopentyloxy group, a 4-cyanopentyloxy group, a 6-cyanohexyloxy group, a 5-cyanohexyloxy group, a 4-cyanohexyloxy group, a 7-cyanoheptyloxy group, a 6-cyanoheptyloxy group, a 5-cyanoheptyloxy group, a 8-cyanoctyloxy group, a 7-cyanoctyloxy group, a 6-cyanoctyloxy group, a 5-cyanoctyloxy group.

-Y in which Q_1 is a "linear or branched lower alkyl group substituted with a hydroxy group" includes more concretely, for example, a 3-hydroxypropyl group, a 4-hydroxybutyl group, a 2-hydroxybutyl group, a 5-hydroxypentyl group, a 4-hydroxypentyl group, a 6-hydroxyhexyl group, a 5-hydroxyhexyl group, a 4-hydroxyhexyl group, a 7-hydroxyheptyl group, a 6-hydroxyheptyl group, a 5-hydroxyheptyl group, a 8-hydroxyoctyl group, a 7-hydroxyoctyl group, a 6-hydroxyoctyl group, a 5-hydroxyoctyl group, a 3-hydroxypropoxy group, a 4-hydroxybutoxy group, a 3-hydroxybutoxy group, a 5-hydroxypentyloxy group, a 4-hydroxypentyloxy group, a 6-hydroxyhexyloxy group, a 5-hydroxyhexyloxy group, a 4-hydroxyhexyloxy group, a 7-hydroxyheptyloxy group, a 6-hydroxyheptyloxy group, a 5-hydroxyheptyloxy group, a 8-hydroxyoctyloxy group, a 7-hydroxyoctyloxy group, a 6-hydroxyoctyloxy group, a 5-hydroxyoctyloxy group.

-Y in which Q_1 is a "linear or branched lower alkyl group substituted with a halogen atom" includes more concretely, for example, a 3-fluoropropyl group, a 4-fluorobutyl group, a 2-fluorobutyl group, a 5-fluoropentyl group, a 4-fluoropentyl group, a 6-fluorohexyl group, a 5-fluorohexyl group, a 4-fluorohexyl group, a 7-fluoroheptyl group, a 6-fluoroheptyl group, a 5-fluoroheptyl group, a 8-fluoroctyl group, a 7-fluoroctyl group, a 6-fluoroctyl group, a 5-fluoroctyl group, a 3-fluoropropoxy group, a 4-fluorobutoxy group, a 3-fluorobutoxy group, a 5-fluoropentyloxy group, a 4-fluoropentyloxy group, a 6-fluorohexyloxy group, a 5-fluorohexyloxy group, a 4-fluorohexyloxy group, a 7-fluoroheptyloxy group, a 6-fluoroheptyloxy group, a 5-fluoroheptyloxy group, a 8-fluoroctyloxy group, a 7-fluoroctyloxy group, a 6-fluoroctyloxy group, a 5-fluoroctyloxy group, a 3-chloropropyl group, a 4-chloropropyl group, a 2-chlorobutyl group, a 5-chloropentyl group, a 4-chloropentyl group, a 6-chlorohexyl group, a 5-chlorohexyl group, a 4-chlorohexyl group, a 7-chloroheptyl group, a

6-chloroheptyl group, a 5-chloroheptyl group, a 8-chlorooctyl group, a 7-chlorooctyl group, a 6-chlorooctyl group, a 5-chlorooctyl group, a 3-chloropropoxy group, a 4-chlorobutoxy group, a 3-chlorobutoxy group, a 5-chloropentyloxy group, a 4-chloropentyloxy group, a 6-chlorohexyloxy group, a 5-chlorohexyloxy group, a 4-chlorohexyloxy group, a 7-chloroheptyloxy group a 6-chloroheptyloxy group, a 5-chloroheptyloxy group, a 8-chlorooctyloxy group, a 7-chlorooctyloxy group, a 6-chlorooctyloxy group, a 5-chlorooctyloxy group.

-Y in which Q_1 is a "linear or branched lower alkyl group substituted with a mono-lower alkylaminocarbonyloxy group" includes more concretely, for example, a 3-(methylcarbamoyloxy)propyl group, a 4-(methylcarbamoyloxy)butyl group, a 3-(methylcarbamoyloxy)butyl group, a

10 5-(methylcarbamoyloxy)pentyl group, a 4-(methylcarbamoyloxy)pentyl group, a
 6-(methylcarbamoyloxy)hexyl group, a 5-(methylcarbamoyloxy)hexyl group, a
 4-(methylcarbamoyloxy)hexyl group, a 7-(methylcarbamoyloxy)heptyl group, a
 6-(methylcarbamoyloxy)heptyl group, a 5-(methylcarbamoyloxy)heptyl group, a
 8-(methylcarbamoyloxy)octyl group, a 7-(methylcarbamoyloxy)octyl group, a
 15 6-(methylcarbamoyloxy)octyl group, a 5-(methylcarbamoyloxy)octyl group.

-Y of formula (IV) in which Q_1 is a "linear or branched lower alkyl group substituted with a di-lower alkylaminocarbonyloxy group" includes more concretely, for example, a

3-(dimethylcarbamoyloxy)propyl group, a 4-(dimethylcarbamoyloxy)butyl group, a
 3-(dimethylcarbamoyloxy)butyl group, a 5-(dimethylcarbamoyloxy)pentyl group, a
 20 4-(dimethylcarbamoyloxy)pentyl group, a 6-(dimethylcarbamoyloxy)hexyl group, a
 5-(dimethylcarbamoyloxy)hexyl group, a 4-(dimethylcarbamoyloxy)hexyl group, a
 2-(dimethylcarbamoyloxy)cycloheptyl group, a 7-(dimethylcarbamoyloxy)heptyl group, a
 6-(dimethylcarbamoyloxy)heptyl group, a 8-(dimethylcarbamoyloxy)octyl group, a
 7-(dimethylcarbamoyloxy)octyl group, a 6-(dimethylcarbamoyloxy)octyl group, a
 25 5-(dimethylcarbamoyloxy)octyl group.

-Y of formula (IV) in which Q_1 is a "linear or branched lower alkyl group substituted with a dialkylcarbamoyl group" includes more concretely, for example, a 3-dimethylcarbamoylpropyl group, a 4-dimethylcarbamoylbutyl group, a 3-dimethylcarbamoylbutyl group, a 5-dimethylcarbamoylpentyl group, a 4-dimethylcabamoylpentyl group, a 6-dimethylcarbamoylhexyl group, a
 30 5-dimethylcarbamoylhexyl group, a 4-dimethylcarbamoylhexyl group, a 7-dimethylcarbamoylheptyl group, a 6-dimethylcarbamoylheptyl group, a 5-dimethylcarbamoylheptyl group, a 8-dimethylcarbamoyloctyl group, a 7-dimethylcarbamoyloctyl group, a 6-dimethylcarbamoyloctyl group, a 5-dimethylcarbamoyloctyl group.

-Y of formula (IV) in which Q_1 is a "linear or branched lower alkyl group substituted with a trifluoromethyl group" includes more concretely, for example, a 3-trifluoropropyl group, a 4-trifluorobutyl group, a 2-trifluorobutyl group, a 5-trifluoropentyl group, a 4-trifluoropentyl group, a 6-trifluorohexyl group, a 5-trifluorohexyl group, a 4-trifluorohexyl group, a 7-trifluoroheptyl group, a 6-trifluoroheptyl group, a 5-trifluoroheptyl group, a 8-trifluoroctyl group, a 7-trifluoroctyl group, a 6-trifluoroctyl group, a 5-trifluoromoctyl group, a 3-trifluoropropoxy group, a 4-trifluorobutoxy group, a

3-trifluorobutoxy group, a 5-trifluoropentyloxy group, a 4-trifluoropentyloxy group, a 6-trifluorohexyloxy group, a 5-trifluorohexyloxy group, a 4-trifluorohexyloxy group, a 7-trifluoroheptyloxy group, a 6-trifluoroheptyloxy group, a 5-trifluoroheptyloxy group, a 8-trifluoroctyloxy group, a 7-trifluoroctyloxy group, a 6-trifluoroctyloxy group, a 5-trifluoroctyloxy group.

5 "Cycloalkyl group having from 3 to 9 carbon atoms" represented by Q_1 may be the same as the cycloalkyl group having from 3 to 9 carbon atoms mentioned hereinabove, more concretely including, for example, a cyclopropyl group, a cyclobutyl group, a cyclopentyl group, a cyclohexyl group, a cycloheptyl group, a cyclooctyl group, a cyclopropylmethyl group, a cyclopropylethyl group, a cyclopropylpropyl group, a cyclopropylbutyl group, a cyclobutylmethyl group, a cyclobutylethyl group, a cyclobutylpropyl group, a cyclobutylbutyl group, a cyclopentylmethyl group, a cyclopentylethyl group, a cyclopentylpropyl group, a cyclopentylbutyl group, a cyclohexylmethyl group, a cyclohexylethyl group, a cyclohexylpropyl group, a cycloheptylmethyl group, a cycloheptylethyl group, a cycloheptylpropyl group, a cycloheptylbutyl group, a cyclopropylmethoxy group, a cyclopropylethoxy group, a cyclopropylpropoxy group, a cyclopropylbutoxy group, a cyclobutylmethoxy group, a cyclobutylethoxy group, a cyclobutylpropoxy group, a cyclobutylbutoxy group, a cyclopentylmethoxy group, a cyclopentylethoxy group, a cyclopentylpropoxy group, a cyclopentylbutoxy group, a cyclopentylpropoxy group, a cyclopentylbutoxy group, a cyclohexylmethoxy group, a cyclohexylethoxy group, a cyclohexylpropoxy group, a cyclohexylbutoxy group, a cyclohexylpropoxy group. Of those, preferred are a cyclopropyl group, a cyclobutyl group, a cyclopentyl group, a cyclohexyl group, a cycloheptyl group; and more preferred are a cyclopropyl group, a cyclobutyl group, a cyclopentyl group, a cyclohexyl group.

20 When Q_1 is a "cycloalkyl group having from 3 to 9 carbon atoms", the substituent which the cycloalkyl group may have is, for example, preferably any of a cyano group, a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxyl group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a lactam ring, a trifluoromethyl group, a mono-lower alkylamino group, a di-lower alkylamino group and an alkanoyl group of the substituents which Q_1 may have; more preferably a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxyl group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a mono-lower alkylamino group, a di-lower alkylamino group or an alkanoyl group. The cycloalkyl group may have one or two such substituents at the bondable position thereof. When the group has two such substituents, then they may be the same or different.

25 -Y of formula (IV) in which Q_1 is a "cycloalkyl group having from 3 to 9 carbon atoms" substituted with any of these substituents includes more concretely, for example, a 2-fluorocyclopropyl group, a 2-chlorocyclopropyl group, a 2,2-difluorocyclopropyl group, a 2-(methoxycarbonyl)cyclopropyl group, a 2-(ethoxycarbonyl)cyclopropyl group, a 2-(propoxycarbonyl)cyclopropyl group, a 2-(tert-butoxycarbonyl)cyclopropyl group, a 2-(methylcarbamoyl)cyclopropyl group, a

2-(ethylcarbamoyl)cyclopropyl group, a 2-(propylcarbamoyl)cyclopropyl group, a
 2-(isopropylcarbamoyl)cyclopropyl group, a 2-(dimethylcarbamoyl)cyclopropyl group, a
 2-(diethylcarbamoyl)cyclopropyl group, a 2-(azetidin-1-ylcarbonyl)cyclopropyl group, a
 2-(pyrrolidin-1-ylcarbonyl)cyclopropyl group, a 2-(piperidin-1-ylcarbonyl)cyclopropyl group, a
 5 2-(2-oxopyrrolidin-1-yl)cyclopropyl group, a 2-(2-oxopiperidin-1-yl)cyclopropyl group, a cyclopentyl
 group, a 2-fluorocyclobutyl group, a 2-chlorocyclobutyl group, a 3-fluorocyclobutyl group, a
 3-chlorocyclobutyl group, a 3,3-difluorocyclobutyl group, a 3-(methoxycarbonyl)cyclobutyl group, a
 3-(ethoxycarbonyl)cyclobutyl group, a 3-(propoxycarbonyl)cyclobutyl group, a
 10 3-(tert-butyloxycarbonyl)cyclobutyl group, a 3-(methylcarbamoyl)cyclobutyl group, a
 3-(ethylcarbamoyl)cyclobutyl group, a 3-(propylcarbamoyl)cyclobutyl group, a
 3-(isopropylcarbamoyl)cyclobutyl group, a 3-(dimethylcarbamoyl)cyclobutyl group, a
 3-(diethylcarbamoyl)cyclobutyl group, a 3-(azetidin-1-ylcarbonyl)cyclobutyl group, a
 3-(pyrrolidin-1-ylcarbonyl)cyclobutyl group, a 3-(piperidin-1-ylcarbonyl)cyclobutyl group, a
 15 3-(2-oxopyrrolidin-1-yl)cyclobutyl group, a 3-(2-oxopiperidin-1-yl)cyclobutyl group, a
 3-fluorocyclopentyl group, a 3-chlorocyclopentyl group, a 3,3-difluorocyclopentyl group, a
 3-(methoxycarbonyl)cyclopentyl group, a 3-(ethoxycarbonyl)cyclopentyl group, a
 3-(propoxycarbonyl)cyclopentyl group, a 3-(tert-butoxycarbonyl)cyclopentyl group, a
 20 3-(methylcarbamoyl)cyclopentyl group, a 3-(ethylcarbamoyl)cyclopentyl group, a
 3-(propylcarbamoyl)cyclopentyl group, a 3-(isopropylcarbamoyl)cyclopentyl group, a
 3-(dimethylcarbamoyl)cyclopentyl group, a 3-(diethylcarbamoyl)cyclopentyl group, a
 3-(azetidin-1-ylcarbonyl)cyclopentyl group, a 3-(pyrrolidin-1-ylcarbonyl)cyclopentyl group, a
 25 3-(piperidin-1-ylcarbonyl)cyclopentyl group, a 3-(2-oxopyrrolidin-1-yl)cyclopentyl group, a
 3-(2-oxopiperidin-1-yl)cyclopentyl group.

When Q_1 is a "phenyl group", the substituent which the phenyl group may have is, for example,
 25 preferably any of a cyano group, a hydroxyl group, a lower alkyl group (the lower alkyl group may be
 substituted with a hydroxyl group, a halogen atom or an amino group), a lower alkoxy group (the lower
 alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower
 alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl
 30 group, a di-lower alkylcarbamoyl group, a carbamoyl group, a lactam ring, a trifluoromethyl group, a
 mono-lower alkylamino group, a di-lower alkylamino group, an alkanoyl group, an alkoxy carbonyl amino
 group (in which the nitrogen atom may be substituted with a lower alkyl group), an alkanoyl amino group
 35 (in which the nitrogen atom may be substituted with a lower alkyl group) and an alkylsulfonyl amino
 group (in which the nitrogen atom may be substituted with a lower alkyl group) of the substituents which
 Q_1 may have; more preferably a hydroxyl group, a lower alkyl group (the lower alkyl group may be
 substituted with a hydroxyl group, a halogen atom or an amino group), a lower alkoxy group (the lower
 alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower
 alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl
 group, a di-lower alkylcarbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a mono-lower
 alkylamino group, a di-lower alkylamino group or an alkanoyl group. The phenyl group may have one

or two such substituents at the bondable position thereof.

3-{(N-methyl)ethoxycarbonylamino}phenyl group, a 2-{(N-methyl)ethoxycarbonylamino}phenyl group, a 4-{(N-methyl)propoxycarbonylamino}phenyl group, a 3-{(N-methyl)propoxycarbonylamino}phenyl group, a 2-{(N-methyl)propoxycarbonylamino}phenyl group, a 4-{(N-methyl)methoxycarbonylamino}phenyl group, a 3-{(N-methyl)methoxycarbonylamino}phenyl group, a 5 4-{(N-methyl)isopropoxycarbonylamino}phenyl group, a 2-{(N-methyl)isopropoxycarbonylamino}phenyl group, a 3-{(N-methyl)isopropoxycarbonylamino}phenyl group, a 2-{(N-methyl)isopropoxycarbonylamino}phenyl group, a 4-{(N-ethyl)methoxycarbonylamino}phenyl group, a 10 2-{(N-ethyl)methoxycarbonylamino}phenyl group, a 4-(acetylamino)phenyl group, a 3-(acetylamino)phenyl group, a 2-(acetylamino)phenyl group, a 4-(propanoylamino)phenyl group, a 3-(propanoylamino)phenyl group, a 2-(propanoylamino)phenyl group, a 4-{(N-methyl)acetylamino}phenyl group, a 3-{(N-methyl)acetylamino}phenyl group, a 2-{(N-methyl)acetylamino}phenyl group, a 4-{(N-ethyl)propanoylamino}phenyl group, a 15 3-{(N-methyl)propanoylamino}phenyl group, a 2-{(methyl)propanoylamino}phenyl group, a 4-{(N-ethyl)propanoylamino}phenyl group, a 3-{(N-ethyl)acetylamino}phenyl group, a 2-{(N-ethyl)acetylamino}phenyl group, a 4-{(M-ethyl)propanoylamino}phenyl group, a 3-{(N-ethyl)propanoylamino}phenyl group, a 2-{(N-ethyl)propanoylamino}phenyl group, a 4-(methylsulfonylamino)phenyl group, a 10 2-(methylsulfonylamino)phenyl group, a 4-(ethylsulfonylamino)phenyl group, a 3-(ethylsulfonylamino)phenyl group, a 2-(ethylsulfonylamino)phenyl group, a 4-(propylsulfonylamino)phenyl group, a 3-(propylsulfonylamino)phenyl group, a 2-(propylsulfonylamino)phenyl group, a 4-(isopropylsulfonylamino)phenyl group, a 3-(isopropylsulfonylamino)phenyl group, a 2-25 4-(isopropylsulfonylamino)phenyl group, a 4-{(N-methyl)methylsulfonylamino}phenyl group, a 3-{(N-methyl)methylsulfonylamino}phenyl group, a 2-{(N-methyl)methylsulfonylamino}phenyl group, a 4-{(N-methyl)ethylsulfonylamino}phenyl group, a 3-{(N-methyl)ethylsulfonylamino}phenyl group, a 2-{(N-methyl)ethylsulfonylamino}phenyl group, a 4-{(N-ethyl)methylsulfonylamino}phenyl group, a 3-{(N-ethyl)methylsulfonylamino}phenyl group, a 2-{(N-ethyl)methylsulfonylamino}phenyl group, a 4-{(N-ethyl)ethylsulfonylamino}phenyl group, a 30 3-{(N-ethyl)ethylsulfonylamino}phenyl group, a 2-{(N-ethyl)ethylsulfonylamino}phenyl group, a 4-{(N-ethyl)propylsulfonylamino}phenyl group, a 3-{(N-ethyl)propylsulfonylamino}phenyl group, a 2-{(N-ethyl)propylsulfonylamino}phenyl group, a 4-(2-oxazolidin-3-yl)phenyl group, a 3-(2-oxazolidin-3-yl)phenyl group, a 2-(oxazolidin-3-yl)phenyl group, a phenylmethyl group, a 4-cyanophenylmethyl group, a 3-cyanophenylmethyl group, a 4-dimethylcarbamoylphenylmethyl group, a 35 3-dimethylcarbamoylphenylmethyl group, a 2-dimethylcarbamoylphenylmethyl group, a 4-methylcarbamoylphenylmethyl group, a 3-methylcarbamoylphenylmethyl group, a 2-methylcarbamoylphenylmethyl group, a 4-cyclopropylcarbamoylphenylmethyl group, a 3-cyclopropylcarbamoylphenylmethyl group, a 2-cyclopropylcarbamoylphenylmethyl group, a 4-(pyrrolidine-1-carbonyl)phenylmethyl group, a 3-(pyrrolidine-1-carbonyl)phenylmethyl group, a

2-(pyrrolidine-1-carbonyl)phenylmethyl group, a 4-(piperidine-1-carbonyl)phenylmethyl group, a 3-(piperidine-1-carbonyl)phenylmethyl group, a 2-(piperidine-1-carbonyl)phenylmethyl group, a 4-(morpholine-1-carbonyl)phenylmethyl group, a 3-(morpholine-1-carbonyl)phenylmethyl group, a 2-(morpholine-1-carbonyl)phenylmethyl group, a 4-chlorophenylmethyl group, a 3-chlorophenylmethyl group, a 2-chlorophenylmethyl group, a 4-hydroxyphenylmethyl group, a 3-hydroxyphenylmethyl group, a 5 2-hydroxyphenylmethyl group, a 4-methylphenylmethyl group, a 3-methylphenylmethyl group, a 2-methylphenylmethyl group, a 4-(trifluoromethyl)phenylmethyl group, a 3-(trifluoromethyl)phenylmethyl group, a 2-(trifluoromethyl)phenylmethyl group, a 4-(2-oxo-2H-pyridin-1-yl)phenylmethyl group, a 4-(3-oxomorpholin-4-yl)phenylmethyl group, a 10 4-(2-oxo-oxazolidin-3-yl)phenylmethyl group, a 4-tert-butylphenylmethyl group, a 3-tert-butylphenylmethyl group, a 2-tert-butylphenylmethyl group, a 4-(trifluoromethoxy)phenylmethyl group, a 3-(trifluoromethoxy)phenylmethyl group, a 2-(trifluoromethyl)phenylmethyl group, a 4-(difluoromethoxy)phenylmethyl group, a 3-(difluoromethoxy)phenylmethyl group, a 4-hydroxyphenylmethyl group, a 3-hydroxyphenylmethyl group, a 2-hydroxyphenylmethyl group, a 15 4-(2-hydroxypropan-2-yl)phenylmethyl group, a 3-(2-hydroxypropan-2-yl)phenylmethyl group, a 4-(methylamino)phenylmethyl group, a 3-(methylamino)phenylmethyl group, a 2-(methylamino)phenylmethyl group, a 4-(dimethylamino)phenylmethyl group, a 3-(dimethylamino)phenylmethyl group, a 2-(dimethylamino)phenylmethyl group, a 4-acetylphenylmethyl group, a 3-acetylphenylmethyl group, a 2-acetylphenylmethyl group, a 4-methanesulfonylphenylmethyl 20 group, a 3-methanesulfonylphenylmethyl group, a 2-methanesulfonylphenylmethyl group, a 4-(acetylamino)phenylmethyl group, a 3-(acetylamino)phenylmethyl group, a 2-(acetylamino)phenylmethyl group, a 4-(N-acetyl-N-methylamino)phenylmethyl group, a 3-(N-acetyl-N-methylamino)phenylmethyl group, a 4-cyano-3-fluorophenylmethyl group, a 25 2-phenylethyl group, a 2-(2-dimethylcarbamoylphenyl)ethyl group, a 2-(4-methylcarbamoylphenyl)ethyl group, a 2-(3-methylcarbamoylphenyl)ethyl group, a 2-(2-methylcarbamoylphenyl)ethyl group, a 2-(4-cyclopropylcarbamoylphenyl)ethyl group, a 2-(3-cyclopropylcarbamoylphenyl)ethyl group, a 2-(2-cyclopropylcarbamoylphenyl)ethyl group, a 2-{4-(pyrrolidine-1-carbonyl)phenyl}ethyl group, a 2-{3-(pyrrolidine-1-carbonyl)phenyl}ethyl group, a 2-{2-(pyrrolidine-1-carbonyl)phenyl}ethyl group, a 30 2-{4-(piperidine-1-carbonyl)phenyl}ethyl group, a 2-{3-piperidine-1-carbonyl)phenyl}ethyl group, a 2-{2-(piperidine-1-carbonyl)phenyl}ethyl group, a 2-{4-(morpholine-1-carbonyl)phenyl}ethyl group, a 2-{3-(morpholine-1-carbonyl)phenyl}ethyl group, a 2-(4-chlorophenyl)ethyl group, a 2-(3-chlorophenyl)ethyl group, a 2-(2-chlorophenyl)ethyl group, a 2-(4-hydroxyphenyl)ethyl group, a 2-(3-hydroxyphenyl)ethyl group, a 2-(2-hydroxyphenyl)ethyl group, a 2-(4-methylphenyl)ethyl group, a 2-(3-methylphenyl)ethyl group, a 2-(2-methylphenyl)ethyl group, a 35 2-{4-(trifluoromethyl)phenyl}ethyl group, a 2-{3-(trifluoromethyl)phenyl}ethyl group, a 2-{2-(trifluoromethyl)phenyl}ethyl group, a 2-{4-(2-oxo-2H-pyridin-1-yl)phenyl}ethyl group, a 2-{4-(3-oxomorpholin-4-yl)phenyl}ethyl group, a 2-{4-(2-oxo-oxazolidin-3-yl)phenyl}ethyl group, a 2-(4-tert-butylphenyl)ethyl group, a 2-(3-tert-butylphenyl)ethyl group, a 2-(2-tert-butylphenyl)ethyl group, a 2-{4-(trifluoromethoxy)phenyl}ethyl group, a 2-{3-(trifluoromethoxy)phenyl}ethyl group, a

2-{2-(trifluoromethyl)phenyl}ethyl group, a 2-{4-(difluoromethoxy)phenyl}ethyl group, a
 2-{3-(difluoromethoxy)phenyl}ethyl group, a 2-(4-hydroxyphenyl)ethyl group, a
 2-(3-hydroxyphenyl)ethyl group, a 2-(2-hydroxyphenyl)ethyl group, a
 2-{4-(2-hydroxypropan-2-yl)phenyl}ethyl group, a 2-{3-(2-hydroxypropan-2-yl)phenyl}ethyl group, a
 5 2-{4-(methylamino)phenyl}ethyl group, a 2-{3-(methylamino)phenyl}ethyl group, a
 2-{2-(methylamino)phenyl}ethyl group, a 2-{4-(dimethylamino)phenyl}ethyl group, a
 2-{3-(dimethylamino)phenyl}ethyl group, a 2-{2-(dimethylamino)phenyl}ethyl group, a
 2-(4-acetylphenyl)ethyl group, a 2-(3-acetylphenyl)ethyl group, a 2-(2-acetylphenyl)ethyl group, a
 2-(4-methanesulfonylphenyl)ethyl group, a 2-(3-methanesulfonylphenyl)ethyl group, a
 10 2-(2-methanesulfonylphenyl)ethyl group, a 2-{4-(acetylamino)phenyl}ethyl group, a
 2-{3-(acetylamino)phenyl}ethyl group, a 2-{2-(acetylamino)phenyl}ethyl group, a
 4-(N-acetyl-N-methylamino)phenylmethyl group, a 2-{3-(N-acetyl-N-methylamino)phenyl}ethyl group,
 a 2-(4-cyano-3-fluorophenyl)ethyl group, a phenoxyethyl group, a 4-cyanophenoxyethyl group, a
 15 3-cyanophenoxyethyl group, a 4-dimethylcarbamoylphenoxyethyl group, a
 3-dimethylcarbamoylphenoxyethyl group, a 2-dimethylcarbamoylphenoxyethyl group, a
 4-methylcarbamoylphenoxyethyl group, a 3-methylcarbamoylphenoxy group, a
 2-methylcarbamoylphenoxyethyl group, a 4-cyclopropylcarbamoylphenoxyethyl group, a
 3-cyclopropylcarbamoylphenoxyethyl group, a 2-cyclopropylcarbamoylphenoxyethyl group, a
 20 4-(pyrrolidine-1-carbonyl)phenoxyethyl group, a 3-(pyrrolidine-1-carbonyl)phenoxyethyl group, a
 2-(pyrrolidine-1-carbonyl)phenoxyethyl group, a 4-(piperidine-1-carbonyl)phenoxyethyl group, a
 3-(piperidine-1-carbonyl)phenoxyethyl group, a 2-(piperidine-1-carbonyl)phenoxyethyl group, a
 4-(morpholine-1-carbonyl)phenoxyethyl group, a 3-(morpholine-1-carbonyl)phenoxyethyl group, a
 2-(morpholine-1-carbonyl)phenoxyethyl group, a 4-chloro-phenoxyethyl group, a
 3-chlorophenoxyethyl group, a 2-chlorophenoxyethyl group, a 4-hydroxyphenylmethyl group, a
 25 3-hydroxyphenylmethyl group, a 2-hydroxyphenoxyethyl group, a 4-methylphenoxyethyl group, a
 3-methylphenoxyethyl group, a 2-methylphenoxyethyl group, a 4-(trifluoromethyl)phenoxyethyl group,
 a 3-(trifluoromethyl)phenoxyethyl group, a 2-(trifluoromethyl)phenoxyethyl group, a
 4-(2-oxo-2H-pyridin-1-yl)phenoxyethyl group, a 4-(3-oxomorpholin-4-yl)phenoxyethyl group, a
 4-(2-oxo-oxazolidin-3-yl)phenoxyethyl group, a 4-tert-butylphenoxyethyl group, a
 30 3-tert-butylphenoxyethyl group, a 2-tert-butylphenoxyethyl group, a
 4-(trifluoromethoxy)phenoxyethyl group, a 3-(trifluoromethoxy)phenoxyethyl group, a
 2-(trifluoromethyl)phenoxyethyl group, a 4-(difluoromethoxy)phenoxyethyl group, a
 3-(difluoromethoxy)phenoxyethyl group, a 4-hydroxyphenoxyethyl group, a
 3-hydroxyphenoxyethyl group, a 2-hydroxyphenoxyethyl group, a
 35 4-(2-hydroxypropan-2-yl)phenoxyethyl group, a 3-(2-hydroxypropan-2-yl)phenoxyethyl group, a
 4-(methylamino)phenoxyethyl group, a 3-(methylamino)phenoxyethyl group, a
 2-(methylamino)phenoxyethyl group, a 4-(dimethylamino)phenoxyethyl group, a
 3-(dimethylamino)phenoxyethyl group, a 2-(dimethylamino)phenoxyethyl group, a
 4-acetylphenylmethyl group, a 3-acetylphenylmethyl group, a 2-acetylphenoxyethyl group, a

4-methanesulfonylphenoxyethyl group, a 3-methanesulfonylphenoxyethyl group, a 2-methanesulfonylphenoxyethyl group, a 4-(acetylamino)phenoxyethyl group, a 3-(acetylamino)phenoxyethyl group, a 2-(acetylamino)phenoxyethyl group, a 4-(N-acetyl-N-methylamino)phenoxyethyl group, a 2-(N-acetyl-N-methylamino)phenoxyethyl group, a 4-cyano-3-fluorophenoxyethyl group.

"5- or 6-membered heteroaryl group" represented by Q_1 means a 5- or 6-membered monocyclic group having from 1 to 3 hetero atoms in the ring, selected from a group consisting of a nitrogen atom, a sulfur atom and an oxygen atom, including, for example, a furyl group, a thienyl group, a pyrrolyl group, an imidazolyl group, a pyrazolyl group, a thiazolyl group, a thiadiazolyl group, an isothiazolyl group, an oxazolyl group, an isoxazolyl group, a pyridyl group, a pyrimidinyl group, a pyrazinyl group. Of those, preferred are a furyl group, a thienyl group, a pyrrolyl group, a pyrazolyl group, a thiazolyl group, a thiadiazolyl group, an isothiazolyl group, an oxazolyl group, an isoxazolyl group, a pyridyl group, a pyrimidinyl group, a pyrazyl group; and more preferred are a pyrazolyl group, a thiazolyl group, a thiadiazolyl group, an isothiazolyl group, an oxazolyl group, an isoxazolyl group, a pyridyl group, a pyrimidinyl group, a pyrazinyl group.

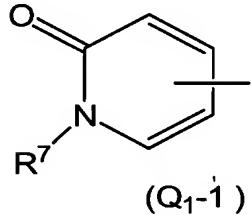
When Q_1 is a "5- or 6-membered heteroaryl group", the substituent which the heteroaryl group may have is, for example, preferably any of a cyano group, a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxyl group, a halogen atom or an amino group), a lower alkyl group, a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a lactam ring, a trifluoromethyl group, a mono-lower alkylamino group, a di-lower alkylamino group and an alkanoyl group of the substituents which Q_1 may have; more preferably a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxyl group, a halogen atom or an amino group), a lower alkyl group, a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a mono-lower alkylamino group, a di-lower alkylamino group or an alkanoyl group. The heteroaryl group may have one or two such substituents at the bondable position thereof.

-Y of formula (IV) in which Q_1 is a "5- or 6-membered heteroaryl group" that may be substituted with any of these substituents includes more concretely, for example, a furyl group, a thienyl group, a pyrrolyl group, an imidazolyl group, a pyrazolyl group, a thiazolyl group, a thiadiazolyl group, an isothiazolyl group, an oxazolyl group, an isoxazolyl group, a pyridyl group, a pyrimidinyl group, a pyrazinyl group, a 6-(pyrrolidine-1-carbonyl)pyridin-3-yl group, a 5-(pyrrolidine-1-carbonyl)pyridin-2-yl group, a 6-(piperidine-1-carbonyl)pyridin-3-yl group, a 5-(piperidine-1-carbonyl)pyridin-2-yl group, a 5-(piperidine-1-carbonyl)pyridin-2-yl group, a 6-methylpyridin-3-yl group, a 5-methylpyridin-2-yl group, a 6-ethylpyridin-3-yl group, a 5-ethylpyridin-2-yl group, a 6-isopropylpyridin-3-yl group, a 5-isopropylpyridin-2-yl group, a 6-cyclopropylpyridin-3-yl group, a 5-cyclopropylpyridin-2-yl group, a 6-fluoropyridin-3-yl group, a 5-fluoropyridin-2-yl group, a 6-(cyclopentyloxy)pyridin-3-yl group, a

5-(cyclopentyloxy)pyridin-2-yl group, a 6-(trifluoromethoxy)pyridin-3-yl group, a 5-(trifluoromethoxy)pyridin-2-yl group, a 6-(difluoromethoxy)pyridin-3-yl group, a 5-(difluoromethoxy)pyridin-2-yl group, a 2-cyanopyridin-5-yl group, a 5-cyanothiophen-2-yl group, a 3-methyl-[1,2,4]oxadiazol-5-yl group.

5 "Heterocyclic group having from 3 to 8 carbon atoms" for Q_1 is described below.

"Heterocyclic group having from 3 to 8 carbon atoms" represented by Q_1 means a 3- to 8-membered monocyclic group having 1 or 2 nitrogen atoms or oxygen atoms in the ring. The heterocyclic group may be the same as the heterocyclic group having from 3 to 8 carbon atoms represented by R which Q_1 may have, or it may be a group of the following formula (Q₁-1):



10

[wherein R⁷ represents a hydrogen atom, a lower alkyl group, a cyclo-lower alkyl group, a halo-lower alkyl group, or an aralkyl group].

When Q_1 is a "heterocyclic group having from 3 to 8 carbon atoms", the substituent which the heterocyclic group may have is, for example, preferably any of a cyano group, a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxyl group, a halogen atom or an amino group), a cyclo-lower alkyl group, a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a lactam ring, a trifluoromethyl group, a mono-lower alkylamino group, a di-lower alkylamino group and an alkanoyl group of the substituents which Q_1 may have; more preferably a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxyl group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a mono-lower alkylamino group, a di-lower alkylamino group or an alkanoyl group. The heterocyclic group may have one or two such substituents at the bondable position thereof.

-Y of formula (IV) in which Q_1 is a "heterocyclic group having from 3 to 8 carbon atoms" that may be substituted with any of these substituents includes more concretely, for example, a 6-oxo-1,6-dihydropyridin-3-yl group, a 6-oxo-1,6-dihydropyridin-4-yl group, a 1-methoxy-6-oxo-1,6-dihydropyridin-3-yl group, a 1-ethoxy-6-oxo-1,6-dihydropyridin-3-yl group, a 1-isopropyl-6-oxo-1,6-dihydropyridin-3-yl group, a 1-(difluoromethyl)-6-oxo-1,6-dihydropyridin-3-yl group, a 1-(2,2-difluoroethyl)-6-oxo-1,6-dihydropyridin-3-yl group, a 1-(2,2,2-trifluoroethyl)-6-oxo-1,6-dihydropyridin-3-yl group, a 1-cyclopropyl-6-oxo-1,6-dihydropyridin-3-yl group, a 1-cyclobutyl-6-oxo-1,6-dihydropyridin-3-yl group, a

1-cyclopentyl-6-oxo-1,6-dihdropyridin-3-yl group, a 1-methyl-6-oxo-1,6-dihdropyridin-4-yl group, a 1-ethy-6-oxo-1,6-dihdropyridin-4-yl group, a 1-isopropyl-6-oxo-1,6-dihdropyridin-4-yl group, a 1-(difluoromethyl)-6-oxo-1,6-dihdropyridin-4-yl group, a 1-(2,2-difluoroethyl)-6-oxo-1,6-dihdropyridin-4-yl group, a 1-(2,2,2-trifluoroethyl)-6-oxo-1,6-dihdropyridin-4-yl group, a 5 1-cyclopropyl-6-oxo-1,6-dihdropyridin-3-yl group, a 1-cyclobutyl-6-oxo-1,6-dihdropyridin-3-yl group, a 1-cyclopropyl-6-oxo-1,6-dihdropyridin-4-yl group, a 1-cyclobutyl-6-oxo-1,6-dihdropyridin-4-yl group, a 1-cyclopentyl-6-oxo-1,6-dihdropyridin-4-yl group, a 1-methy-2-oxo-1,2-dihdropyridin-3-yl group, a 1-ethy-2-oxo-1,2-dihdropyridin-3-yl group, a 1-cyclopentyl-2-oxo-1,2-dihdropyridin-3-yl group, a 1-cyclopentyl-2-oxo-1,2-dihdropyridin-3-yl group.

10 When Q_1 is a "naphthyl group", the substituent which the naphthyl group may have is, for example, preferably any of a cyano group, a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxyl group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a lactam ring, a trifluoromethyl group, a 15 mono-lower alkylamino group, a di-lower alkylamino group and an alkanoyl group of the substituents which Q_1 may have; more preferably a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxyl group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a mono-lower 20 alkylamino group, a di-lower alkylamino group or an alkanoyl group. The naphthyl group may have one or two such substituents at the bondable position thereof.

-Y of formula (IV) in which Q_1 is a "naphthyl group" that may be substituted with any of these 25 substituents includes more concretely, for example, a 5-cyanonaphthalen-1-yl group, a 6-cyanonaphthalen-1-yl group, a 7-cyanonaphthalen-1-yl group, a 5-cyanonaphthalen-2-yl group, a 6-cyanonaphthalen-2-yl group, a 7-cyanonaphthalen-2-yl group, a 5-fluoronaphthalen-1-yl group, a 6-fluoronaphthalen-1-yl group, a 7-fluoronaphthalen-1-yl group, a 5-fluoronaphthalen-2-yl group, a 6-fluoronaphthalen-2-yl group, a 7-fluoronaphthalen-2-yl group, a 5-methoxynaphthalen-1-yl group, a 30 6-methoxynaphthalen-1-yl group, a 7-methoxynaphthalen-1-yl group, a 5-methoxynaphthalen-2-yl group, a 6-methoxynaphthalen-2-yl group, a 7-methoxynaphthalen-2-yl group, a 5-hydroxynaphthalen-1-yl group, a 6-hydroxynaphthalen-1-yl group, a 7-hydroxynaphthalen-1-yl group, a 5-hydroxynaphthalen-2-yl group, a 6-hydroxynaphthalen-2-yl group, a 7-hydroxynaphthalen-2-yl group, a 35 5-methylsulfonylnaphthalen-1-yl group, a 6-methylsulfonylnaphthalen-1-yl group, a 7-methylsulfonylnaphthalen-1-yl group, a 5-methylsulfonylnaphthalen-2-yl group, a 6-methylsulfonylnaphthalen-2-yl group, a 7-methylsulfonylnaphthalen-2-yl group, a 5-trifluoromethylnaphthalen-1-yl group, a 6-trifluoromethylnaphthalen-1-yl group, a 7-trifluoromethylnaphthalen-1-yl group, a 5-trifluoromethylnaphthalen-2-yl group, a 6-trifluoromethylnaphthalen-2-yl group, a 7-trifluoromethylnaphthalen-2-yl group.

"Condensed-cyclic heteroaryl group" represented by Q_1 means a bicyclic group formed through condensation of a benzene or pyridine ring with a 5- to 7-membered monocyclic ring having from 1 to 3 hetero atoms selected from a group consisting of an oxygen atom, a sulfur atom and a nitrogen atom, or means a tricyclic group that comprises the bicyclic ring and a benzene or pyridine ring bonding thereto.

5 "Condensed-cyclic heteroaryl group" represented by Q_1 includes, for example, a benzofuranyl group, an indolyl group, a quinolinyl group, an isoquinolinyl group, a benzoxazolyl group, a benzimidazolyl group, a phthalazinyl group, a naphthyridinyl group, a quinoxaliny group, a quinazolinyl group, a cinnolinyl group, an imidazopyridinyl group. Of those, preferred are a benzofuranyl group, an indolyl group, a quinolinyl group, an isoquinolinyl group, a benzoxazolyl group, a benzimidazolyl group, 10 a phthalazinyl group, a naphthyridinyl group, a quinoxaliny group, a quinazolinyl group, a cinnolinyl group, an imidazopyridinyl group; and more preferred are a quinolinyl group, an isoquinolinyl group, a benzoxazolyl group, a benzimidazolyl group, a phthalazinyl group, a naphthyridinyl group, a quinoxaliny group, a quinazolinyl group, a cinnolinyl group, an imidazopyridinyl group.

15 When Q_1 is a "condensed-cyclic heteroaryl group", the substituent which the condensed-cyclic heteroaryl group may have is, for example, preferably any of a cyano group, a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxyl group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a 20 mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a lactam ring, a trifluoromethyl group, a mono-lower alkylamino group, a di-lower alkylamino group and an alkanoyl group of the substituents which Q_1 may have; more preferably a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxyl group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower 25 alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a mono-lower alkylamino group, a di-lower alkylamino group or an alkanoyl group. The condensed-cyclic heteroaryl group may have one or two such substituents at the bondable position thereof.

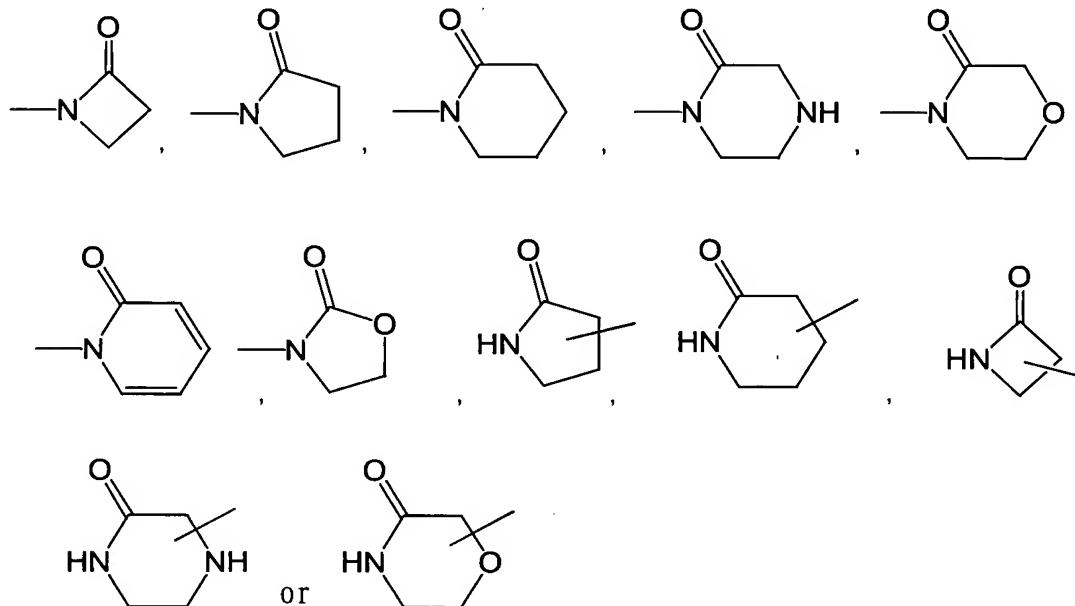
30 -Y of formula (IV) in which Q_1 is a "naphthyl group" that may be substituted with any of these substituents includes more concretely, for example, a quinolin-3-yl group, a quinolin-2-yl group, a 1H-indol-6-yl group, a 1H-indol-7-yl group, an indolin-2-on-6-yl group, an indolin-2-on-7-yl group, a 1-methylindolin-2-on-6-yl group, a 1-methylindolin-2-on-7-yl group, a 1-ethylindolin-2-on-6-yl group, a 1-ethylindolin-2-on-7-yl group, a 1-(difluoromethyl)indolin-2-on-6-yl group, a 35 1-(difluoromethyl)indolin-2-on-7-yl group, a quinolin-8-yl group, a quinolin-7-yl group, a dibenzofuran-3-yl group, a dibenzothiophen-3-yl group.

When Q_1 is a linear or branched lower alkyl group, a phenyl group, a 5- or 6-membered heteroaryl group, a heterocyclic group having from 3 to 8 carbon atoms (in which the hetero ring has 1 or 2 nitrogen atoms or oxygen atoms), a naphthyl group or a condensed-cyclic heteroaryl group, which may be substituted, and when the substituent which Q_1 may have is a "lactam ring", the lactam ring means a 3-

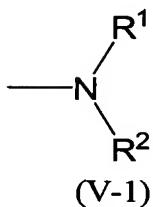
to 9-membered monocyclic group having a group of $-N(R^3)-C(O)-$ in the ring, and it may have 1 or 2 carbon-carbon double bonds. (In this, R^3 represents a hydrogen atom or a lower alkyl group.)

Except the nitrogen atom that constitutes $-N-C(O)-$ in the lactam ring, the ring may have 1 or 2 oxygen atoms or nitrogen atoms. The position of the lactam ring that bonds to Q_1 is not specifically defined, and the ring may bond to it at any bondable position thereof.

More concretely, the lactam ring includes, for example, those of the following formulae:



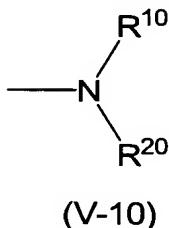
When Q_1 is a group of the above-mentioned formula (V-1):



10

(wherein the symbols have the same meanings as above), the group is described below.

Of the group of formula (V-1), Q_1 is preferably a group of a formula (V-10):



(wherein the symbols have the same meanings as above).

15

"Alkyl group having from 1 to 6 carbon atoms" represented by R^1 and R^2 in formula (V-1) for Q_1 may be the same linear or branched alkyl group as that mentioned hereinabove. Of those, the lower alkyl group is preferably a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, a sec-butyl group, a tert-butyl group, a pentyl group, an isoamyl group, a

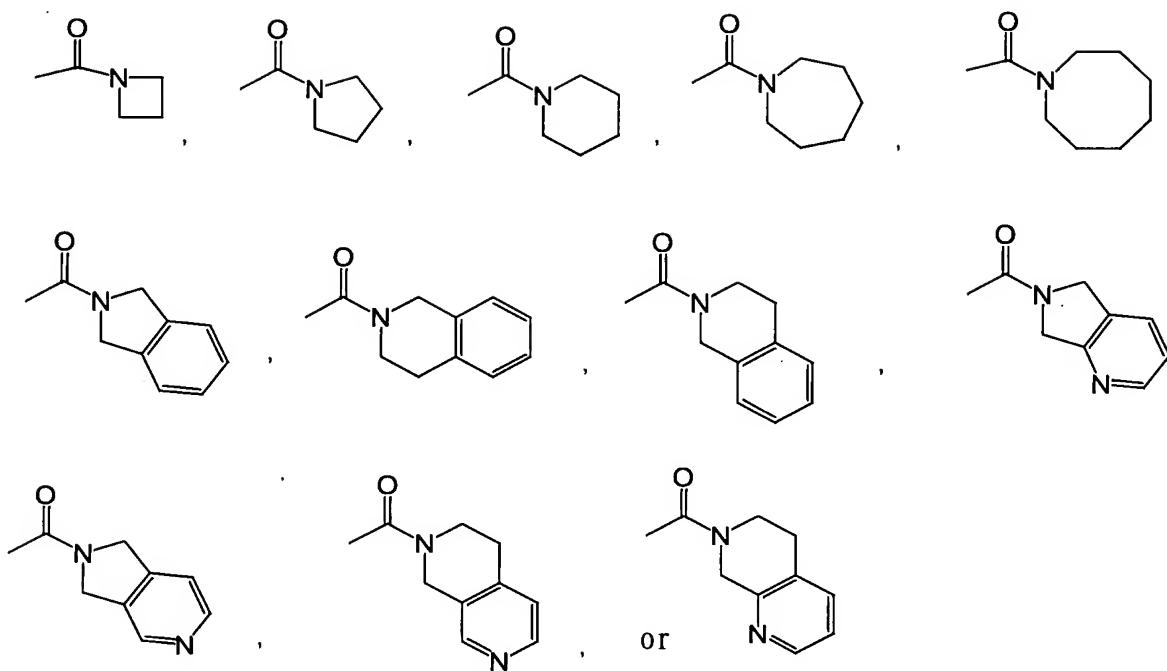
neopentyl group, a hexyl group or an isohexyl group, more preferably a methyl group, an ethyl group, a propyl group, an isopropyl group, a butyl group, an isobutyl group, a pentyl group, an isoamyl group, a neopentyl group or a hexyl group.

-Y of formula (IV) in which Q_1 is a group of formula (V-1) and R^1 and R^2 are the same or different, each representing a lower alkyl group, includes more concretely, for example, an N,N-diethylamino group, an N,N-dipropylamino group, an N,N-diisopropylamino group, an N,N-dibutylamino group, an N,N-dipentylamino group, an N,N-dihexylamino group, an N,N-diheptylamino group, an N-methyl-N-ethylamino group, an N-methyl-N-propylamino group, an N-methyl-N-isopropylamino group, an N-methyl-N-butylamino group, an N-methyl-N-pentylamino group, an N-methyl-N-hexylamino group, an N-methyl-N-heptylamino group, an N-ethyl-N-propylamino group, an N-ethyl-N-isopropylamino group, an N-ethyl-N-butylamino group, an N-ethyl-N-pentylamino group, an N-ethyl-N-hexylamino group, an N-ethyl-N-heptylamino group.

"Mono-lower alkylcarbamoyl group" represented by R^1 and R^2 in formula (V-1) for Q_1 may have the same meaning as the above-defined "mono-lower alkylcarbamoyl group". Of those, preferred are a methylcarbamoyl group, an ethylcarbamoyl group, a propylcarbamoyl group, an isopropylcarbamoyl group, a butylcarbamoyl group, a sec-butylcarbamoyl group, a tert-butylcarbamoyl group; and more preferred are a methylcarbamoyl group, an ethylcarbamoyl group, a propylcarbamoyl group, an isopropylcarbamoyl group, a tert-butylcarbamoyl group.

"Di-lower alkylcarbamoyl group" represented by R^1 and R^2 in formula (V-1) for Q_1 means a carbamoyl group di-substituted with the above-mentioned, same or different lower alkyl groups. "Di-lower alkylcarbamoyl group" includes, for example, a dimethylcarbamoyl group, a diethylcarbamoyl group, an ethylmethylcarbamoyl group, a dipropylcarbamoyl group, a methylpropylcarbamoyl group, a diisopropylcarbamoyl group.

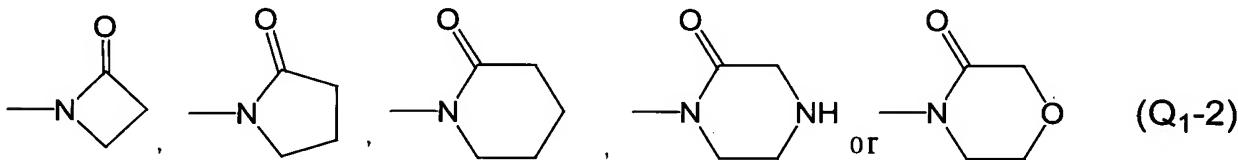
The "di-lower alkylcarbamoyl group" may include a 5- to 8-membered monocyclic structure formed by the nitrogen atom of the carbamoyl group and the same or different lower alkyl groups bonding to the nitrogen atom, and may include a bicyclic structure formed through condensation of the monocyclic structure and a benzene or pyridine ring. Concretely, it may include groups of the following formulae:

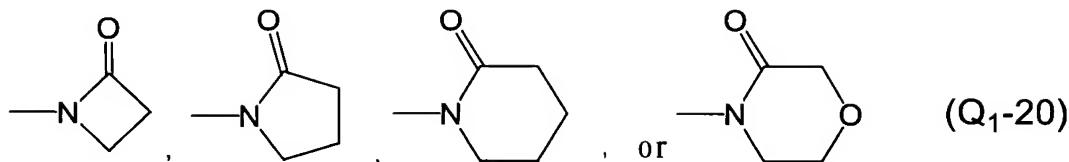


When R_1 and R_2 in formula (V-1) for Q^1 each represents "a lower alkyl group or a mono- or di-lower alkylcarbamoyl group", they may be the same or different.

-Y of formula (IV) in which Q_1 is a group of formula (V-1) and R^1 and R^2 are the same or different, each representing a lower alkyl group or a mono- or di-lower alkylcarbamoyl group, includes more concretely, for example, an N-methyl-N-(dimethylcarbamoylmethyl)amino group, an N-methyl-N-(dimethylcarbamoylethyl)amino group, an N-methyl-N-(diethylcarbamoylmethyl)amino group, an N-methyl-N-(diethylcarbamoylethyl)amino group, an N-methyl-N-(dimethylcarbamoylmethyl)aminomethyl group, an N-methyl-N-(dimethylcarbamoylethyl)aminomethyl group, an N-methyl-N-(dimethylcarbamoylmethyl)aminoethyl group, an N-methyl-N-(diethylcarbamoylmethyl)aminoethyl group.

When Q_1 is a group of formula (V-1) and when R^1 and R^2 form, along with the nitrogen atom adjacent thereto, a 3- to 9-membered lactam ring, then the "3- to 9-membered lactam ring" means a 3- to 9-membered group containing a group of $-N-C(O)-$ in the ring, and it may have 1 or 2 oxygen atoms or nitrogen atoms in addition to the nitrogen atom that constitutes the group of $-N-C(O)-$ in the lactam ring. The lactam ring includes, for example, groups of the following formula (Q₁-2):





-Y of formula (IV) in which Q₁ is a group of formula (V-1) and R¹ and R² are the same or different, each representing a lower alkylcarbamoyl group, includes more concretely, for example, a 5 2-oxo-2H-pyridin-1-yl group, a 2-oxo-pyrolidin-1-yl group, a 2-oxo-piperidin-1-yl group, a 2-oxo-homopiperidin-1-yl group, a 2-oxo-heptamethyleneimin-1-yl group, a 2-oxo-morpholin-1-yl group, a 2-oxo homomorpholin-1-yl group, a 2-oxo-2H-pyridin-1-yl methyl group, a 2-oxo-pyrolidin-1-ylmethyl group, a 2-oxo-piperidin-1-ylmethyl group, a 2-oxo-homopiperidin-1-ylmethyl group, a 2-oxo-heptamethyleneimin-1-ylmethyl group, a 2-oxo-morpholin-1-ylmethyl group, a 2-oxo homomorpholin-1-ylmethyl group, a 2-oxo-2H-pyridine-1-yl group, a 2-oxo-pyrolidine-1-yl group, a 2-oxo-piperidine-1-ylethyl group, a 2-oxo-homopiperidin-1-ylethyl group, a 2-oxo-heptamethyleneimin-1-ylethyl group, a 2-oxo-morpholin-1-ylethyl group, a 2-oxo homomorpholin-1-ylethyl group,

15 When Q₁ is a group of formula (V-1) and when R¹ and R² form, along with the nitrogen atom adjacent thereto, a heterocyclic group having from 3 to 8 carbon atoms, the "heterocyclic group having from 3 to 8 carbon atoms" means a 3- to 8-membered heterocyclic group having 1 or 2 nitrogen atoms or oxygen atoms as the constitutive atoms of the hetero ring, and it includes, for example, an azetidinyl group, a pyrrolidinyl group, a piperidinyl group, a homopiperidinyl group, a heptamethyleneiminyl group, a morpholinyl group, a homomorpholinyl group. Of those, preferred are a piperidinyl group, a 20 homopiperidinyl group, a heptamethyleneiminyl group, a morpholinyl group, a homomorpholinyl group.

-Y of formula (IV) in which Q₁ is a group of formula (V-1) and R¹ and R² form, along with the nitrogen atom adjacent thereto, a heterocyclic group having from 3 to 8 carbon atoms (which has 1 or 2 nitrogen atoms or oxygen atoms as the constitutive atoms of the ring) includes more concretely, for example, a morpholin-1-yl group, a homomorpholin-1-yl group, a morpholin-1-ylmethyl group, a homomorpholin-1-ylmethyl group, a 25 2-(morpholin-1-yl)ethyl group, a 2-(homomorpholin-1-yl)ethyl group, a 3-(morpholin-1-yl)propyl group, a 3-(homomorpholin-1-yl)propyl group.

When Q₁ is a group of formula (V-1) and when R¹ and R² form, along with the nitrogen atom adjacent thereto, a 5-membered heteroaryl group, the "5-membered heteroaryl group" means a 30 5-membered monocyclic group having the same or different, from 1 to 4 hetero atoms selected from a nitrogen atom, a sulfur atom and an oxygen atom in the ring, and it includes, for example, a pyrrolyl group, an imidazolyl group, a pyrazolyl group, a triazolyl group, a tetrazolyl group, an oxazolyl group, a thiazolyl group, a thiadiazolyl group. Of those, preferred are pyrazole, triazole, tetrazole, oxazole, thiazole, thiadiazole; and more preferred are pyrazole, triazole, oxazole, thiazole, thiadiazole.

-Y of formula (IV) in which Q₁ is a group of formula (V-1) and R¹ and R² form, along with the 35 nitrogen atom adjacent thereto, a 5-membered heteroaryl group, includes more concretely, for example, a

pyrazol-1-yl group, a 3-phenylpyrazol-1-yl group, a 4-phenylpyrazol-1-yl group, a 5-phenylpyrazol-1-yl group, a triazol-1-yl group, a tetrazol-1-yl group, a pyrazol-1-ylmethyl group, a triazol-1-ylmethyl group, a tetrazol-1-ylmethyl group, a 2-(pyrazol-1-yl)ethyl group, a 2-(triazol-1-yl)ethyl group, a 2-(tetrazol-1-yl)ethyl group.

5 -Y of formula (IV) in which Q₁ is a group of formula (V-1) and R¹ and R² form, along with the nitrogen atom adjacent thereto, a condensed-cyclic heteroaryl group, includes more concretely, for example, a benzimidazol-1-yl group, a 6-cyanobenzimidazol-1-yl group, a 7-cyanobenzimidazol-1-yl group, a 6-(trifluoromethyl)benzimidazol-1-yl group, a 7-(trifluoromethyl)benzimidazol-1-yl group, a 6-phenylbenzimidazol-1-yl group, a 7-phenylbenzimidazol-1-yl group, a benzotriazol-1-yl group, a 10 benzotriazol-2-yl group, an imidazo[1,5,b]pyridin-6-yl group, a benzimidazol-1-ylmethyl group, a benzotriazol-1-ylmethyl group, a benzotriazol-2-ylmethyl group, an imidazo[1,5,b]pyridin-6-ylmethyl group, a 2-(benzimidazol-1-yl)ethyl group, a 2-(benzotriazol-1-yl)ethyl group, a 2-(benzotriazol-2-yl)ethyl group, a 2-(imidazo[1,5,b]pyridin-1-yl)ethyl group.

More concretely, the compounds (I) of the invention include, for example,

15 2-(1-cyclopentylpyridin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,
 2-(1-isopropylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,
 2-(1-cyclopentylpyrrolidin-3-yloxy)-5-(4-carbamoylphenyl)pyrimidine,
 2-(1-cyclopentylpyrrolidin-3-yloxy)-5-(4-cyanophenyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{(4-methyl-1,3,5-oxadiazol-2-yl)phenyl}pyrimidine,

20 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyridine,
 2-(1-cyclobutylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,
 2-(1-cyclohexylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,
 2-(1-cyclopropylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,
 2-(1-ethylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine,

25 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(pyrrolidin-1-ylcarbonyl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(dimethylcarbamoyl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(morpholin-4-ylcarbonyl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(phenoxy)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(3-quinolinyl)pyrimidine,

30 2-(1-cyclopentylpiperidin-4-yloxy)-5-{5-indolyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(pyridon-1-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(piperidon-1-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(3-quinolinyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-phenyl-4-hydroxypiperidin-1-yl)pyrimidine,

35 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-methoxypyridin-5-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-chlorophenyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-trifluoromethylphenyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(3-pyridinyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-methoxyphenyl)pyrimidine,

2-(1-cyclopentylpiperidin-4-yloxy)-5-(dibenzofuran-4-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-cyclopentyloxypyridin-5-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-pyridon-5-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(1-cyclopentyl-2-pyridon-3-yl)pyrimidine,
 5 2-(1-cyclopentylpiperidin-4-yloxy)-5-{2-(pyrrolidin-1-ylcarbonyl)pyridin-5-yl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-cyano-5-thenyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(oxomorpholin-4-yl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(2-oxazolidinon-3-yl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-methyl-3-pyridin-5-yl)pyrimidine,
 10 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-fluoro-3-pyridin-5-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(2-pyridon-1-yl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(methylsulfonyl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-acetylphenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-trifluoromethoxyphenyl)pyrimidine,
 15 2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(2-hydroxy-2-propyl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-ethylpyridin-5-yl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrazine,
 5-(1-cyclopentylpiperidin-4-yloxy)-2-(4-cyanophenyl)pyridine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyridazine,
 20 2-(1-cyclopentylpiperidin-4-yloxy)-5-(piperidin-1-ylcarbonyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(piperidin-1-ylmethyl)phenyl}pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-phenylpiperazin-1-ylmethyl)pyrimidine,
 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-cyanopyrimidin-5-yl)pyrimidine.

The compounds (I) of the invention have an effect as a histamine-H3 acceptor antagonist or
 25 inverse-agonist.

"Histamine-H3 receptor inverse-agonist" as referred to herein means a receptor-binding substrate that has an effect completely or partially opposite to the effect of a histamine-H3 receptor agonist, and is a ligand capable of inhibiting the homeostatic activity of a histamine-H3 receptor.

[Best Mode for Carrying out the Invention]

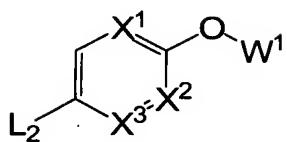
30 Methods for producing the compounds of the invention are described below.

The compounds (I) of the invention may be readily produced, using any known reaction methods or according to any per-se known methods. The compounds (I) of the invention may be produced not only according to ordinary liquid-phase production methods but also according to any solid-phase methods such as combinatorial production methods or parallel production methods that are
 35 being significantly developed these days.

The compounds of the invention may be produced, for example, according to the methods mentioned below.

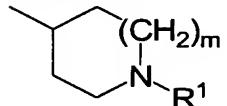
Production Method 1

A compound of a general formula (VI):



(VI)

[wherein W¹ represents a group of the following formula (II-1):

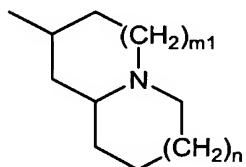


(II-1)

(wherein m indicates an integer of from 0 to 3; R¹ represents a linear or branched lower alkyl group

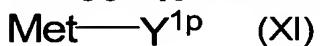
5 (excepting a methyl group), a cycloalkyl group having from 3 to 9 carbon atoms, an aralkyl group or a heterocyclic group having from 3 to 8 carbon atoms (the hetero ring has 1 or 2 nitrogen atoms or oxygen atoms), which may be substituted with a group selected from a class consisting of a cyano group, a hydroxyl group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxyl group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a cycloalkyliminocarbonyl group and a trifluoromethyl group, or represents a group corresponding to R but having a protective group suitably introduced into the substituent which R has), or represents a group or a formula (III):

10

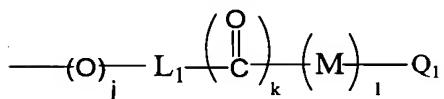


(III)

15 (wherein m1 indicates an integer of from 0 to 3; n indicates an integer of from 0 to 2); and L₃ represents a leaving group], is reacted with a compound of a general formula (XI):



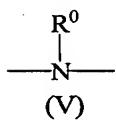
[wherein Met represents a general organic metal atom; Y^{1P} represents a group of a formula (IV):



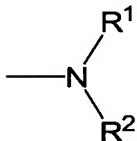
20

(IV)

(wherein j, k and l each independently indicate 0 or 1; L₁ represents a lower alkylene group having from 1 to 4 carbon atoms, or a single bond; M represents an oxygen atom or a group of a formula (V):

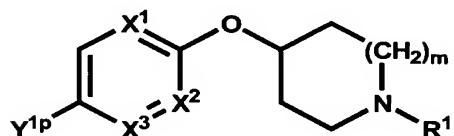


(wherein R^0 represents a lower alkyl group having from 1 to 4 carbon atoms); Q_1 represents a linear or branched lower alkyl group, a cycloalkyl group having from 3 to 9 carbon atoms, a phenyl group, a 5-membered or 6-membered heteroaryl group, a heterocyclic group having from 3 to 8 carbon atoms (the hetero ring may have 1 or 2 nitrogen atoms or oxygen atoms), a naphthyl group or a condensed-cyclic heteroaryl group, which may be substituted with a group selected from a class consisting of a cyano group, a hydroxy group, a lower alkyl group (the lower alkyl group may be substituted with a hydroxy group, a halogen atom or an amino group), a lower alkoxy group (the lower alkoxy group may be substituted with a halogen atom), a lower alkylsulfonyl group, a cyclo-lower alkylsulfonyl group, a halogen atom, a mono-lower alkylaminocarbonyloxy group, a di-lower alkylaminocarbonyloxy group, a mono-lower alkylcarbamoyl group, a di-lower alkylcarbamoyl group, a carbamoyl group, a cycloalkyliminocarbamoyl group, a lactam ring, a trifluoromethyl group, a mono-lower alkylamino group, a di-lower alkylamino group and an alkanoyl group, or represents a group corresponding to Q_1 but having a protective group optionally introduced into the substituent which Q_1 has, or represents a group of a formula (V-1):



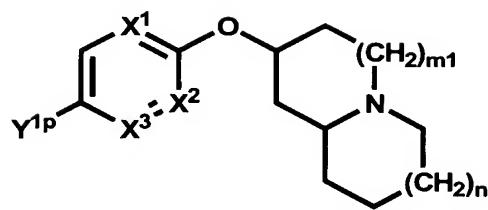
15 (V-1)

(wherein R^1 and R^2 are the same or different, each representing a lower alkyl group or a mono- or di-lower alkylcarbamoyl group, or R^1 and R^2 together form, along with the adjacent nitrogen atom, a 3- to 9-membered lactam ring, a heterocyclic group having from 3 to 8 carbon atoms (the group has 1 or 2 nitrogen atoms or oxygen atoms in the ring thereof), a 5-membered heteroaryl group or a condensed-cyclic heteroaryl group), or represents a group corresponding to $-\text{Y}$ but having a protective group optionally introduced into the substituent which $-\text{Y}$ has], in the presence of a catalyst, to give a compound of a general formula (VIII):



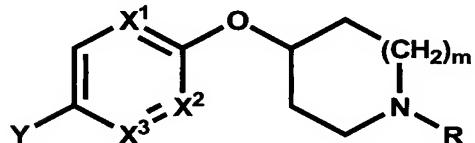
(VIII)

[wherein X^1 , X^2 , X^3 , m , R^1 and Y^{1p} have the same meanings as above], or a compound of a general formula (IX):



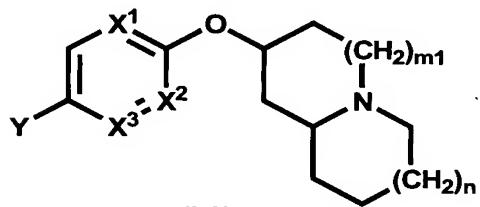
(IX)

[wherein X^1 , X^2 , X^3 , m^1 , n and Y^{1p} have the same meanings as above], and optionally the protective group is removed to give a compound of a general formula (I-2):



(I-2)

5 [wherein X^1 , X^2 , X^3 , m , R and Y have the same meanings as above], or a compound of a general formula (I-3):



(I-3)

[wherein X^1 , X^2 , X^3 , m^1 , n and Y have the same meanings as above].

The general organic metal atom of Met means an organic metal atom generally used in cross-coupling reaction, including, for example, lithium, boron, silicon, magnesium, aluminium, zinc, tin, more preferably boron, zinc, and tin. Regarding the concrete embodiments of its use, for example, boron may be used as boric acid or borates; zinc may be used as zinc chloride, zinc bromide or zinc iodide; and tin may be used as tri-lower alkyl-tin.

The leaving group for L_2 may be any one having the function of leaving in the reaction of the compounds of formulae (VI) and (VII). More concretely, Y^{1p} includes, for example, a halogen atom such as a chlorine atom, a bromine atom or an iodine atom; an organic sulfonyl group such as a methanesulfonyl group, an ethanesulfonyl group, a benzenesulfonyl group; and an organic sulfonyloxy group such as a methanesulfonyloxy group, a trifluoromethanesulfonyloxy group, and a p-toluenesulfonyloxy group.

Regarding the reaction between the compound of formula (VI) and the compound of formula (VII), in general, from 0.5 mols to 5 mols, preferably from 0.7 mols to 3 mols of the compound (VII) is reacted with 1 mol of the compound (X).

The catalyst to be used in the reaction is, for example, a transition metal generally used in cross-coupling, such as copper, nickel, palladium. More concretely, preferred are tetrakis(triphenylphosphine)palladium(0), palladium(II) acetate, bis(triphenylphosphine)palladium(II) chloride, [1,1'-bis(diphenylphosphino)ferrocene]palladium(II) dichloride.

The reaction is effected generally in an inert solvent. The inert solvent is, for example, preferably water, benzene, toluene, xylene, methylene chloride, chloroform, dimethoxyethane, tetrahydrofuran, dioxane, dimethylformamide, and their mixed solvents.

5 The reaction temperature may be generally from room temperature to the boiling point of the solvent used in the reaction, preferably from 20°C to 200°C.

The reaction time may be generally from 30 minutes to 7 days, preferably from 3 hours to 2 days.

10 Preferably, the reaction is effected in the presence of a base. The base includes, for example, an inorganic base such as sodium hydroxide, potassium hydroxide, sodium hydrogencarbonate, sodium carbonate, potassium carbonate, cesium carbonate; and an organic base such as triethylamine, diisopropylamine.

The amount of the base to be used may be generally from 0.5 mols to 5 mols, preferably from 0.7 mols to 3 mols relative to 1 mol of the compound of formula (VI).

15 After the reaction, when the reaction product has a protective group, then the protective group is removed, but when the reaction product does not have a protective group, then it may be directly processed in an ordinary manner to obtain a compound (I-2) or (I-3) of the invention.

Thus obtained, the compound (I-2) or (I-3) of the invention may be isolated and purified in any known isolation and purification method, for example, through concentration, reduced-pressure concentration, recrystallization, reprecipitation, solvent extraction or chromatography.

20 The compounds of formulae (VI), (VII), (IX) and (X) may be commercially-available ones, or may be prepared in any known methods or according to such known methods, or according to the methods described in Examples and Reference Examples given hereinunder, optionally suitably combining any of such methods.

25 In the above-mentioned reaction, when the reactants have a group not participating in the reaction, such as an amino group, an imino group, a hydroxyl group, a carboxyl group, an oxo group or a carbonyl group, then the amino group, the imino group, the hydroxyl group, the carboxyl group, the oxo group or the carbonyl group may be suitably protected with a protective group for the amino group or the imino group, or a protective group for the hydroxyl group, or a protective group for the carboxyl group, or a protective group for the oxo group or the carbonyl group, and then the reaction may be effected, and, 30 after the reaction, the protective group may be removed. The introduction and the removal of the protective group may be attained according to the methods described in *Protective Groups in Organic Synthesis* mentioned above, or according to methods similar to these, or by combining any of such methods.

35 "Protective group for amino group or imino group" is not specifically defined, so long as the group has its own function. For example, preferred are an aralkyl group such as a benzyl group, a p-methoxybenzyl group, a 3,4-dimethoxybenzyl group, an o-nitrobenzyl group, a p-nitrobenzyl group, a benzhydryl group, a trityl group; a lower alkanoyl group such as a formyl group, an acetyl group, a propionyl group, a butyryl group, a pivaloyl group; a benzoyl group; an arylalkanoyl group such as a phenylacetyl group, a phenoxyacetyl group; a lower alkoxy carbonyl group such as a methoxycarbonyl

group, an ethoxycarbonyl group, a propyloxycarbonyl group, a tert-butoxycarbonyl group; an aralkyloxycarbonyl group such as a benzyloxycarbonyl group, a p-nitrobenzyloxycarbonyl group, a phenethyloxycarbonyl group; a lower alkylsilyl group such as a trimethylsilyl group, a tert-butyldimethylsilyl group; a tetrahydropyranyl group; a trimethylsilylethoxymethyl group; a lower alkylsulfonyl group such as a methylsulfonyl group, an ethylsulfonyl group; an arylsulfonyl group such as a benzenesulfonyl group, a toluenesulfonyl group; and more preferred are an acetyl group, a benzoyl group, a tert-butoxycarbonyl group, a trimethylsilylethoxymethyl group, a methylsulfonyl group.

"Protective group for hydroxyl group" is not specifically defined, so long as the group has its own function. For example, preferred are a lower alkyl group such as a methyl group, an ethyl group, a propyl group, an isopropyl group, a tert-butyl group; a lower alkylsilyl group such as a trimethylsilyl group, a tert-butyldimethylsilyl group; a lower alkoxyethyl group such as a methoxymethyl group, a 2-methoxyethoxymethyl group; a tetrahydropyranyl group; a trimethylsilylethoxymethyl group; an aralkyl group such as a benzyl group, a p-methoxybenzyl group, a 2,3-dimethoxybenzyl group, an o-nitrobenzyl group, a p-nitrobenzyl group, a trityl group; an acyl group such as a formyl group, an acetyl group; and more preferred are a methyl group, a methoxymethyl group, a tetrahydropyranyl group, a trityl group, a trimethylsilylethoxymethyl group, a tert-butyldimethylsilyl group, an acetyl group.

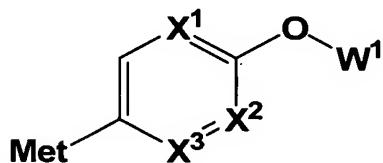
"Protective group for carboxyl group" is not specifically defined, so long as the group has its own function. For example, preferred are a lower alkyl group such as a methyl group, an ethyl group, a propyl group, an isopropyl group, a tert-butyl group; a halo-lower alkyl group such as a 2,2,2-trichloroethyl group; a lower alkenyl group such as a 2-propenyl group; an aralkyl group such as a benzyl group, a p-methoxybenzyl group, a p-nitrobenzyl group, a benzhydryl group, a trityl group; and more preferred are a methyl group, an ethyl group, a tert-butyl group, a 2-propenyl group, a benzyl group, a p-methoxybenzyl group, a benzhydryl group.

"Protective group for oxo group or carbonyl group" is not specifically defined, so long as the group has its own function. For example, it includes acetals and ketals such as ethylene ketal, trimethylene ketal, dimethyl ketal.

The compounds of the invention may also be produced according to the following method.

Production Method 2

A compound of a general formula (X):



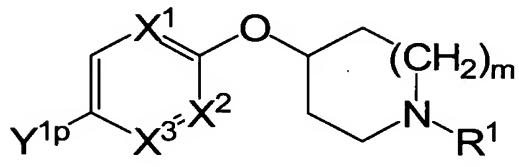
(X)

30

[wherein X¹, X², X³, W¹ and Met have the same meanings as above] is reacted with a compound of a general formula (XI):

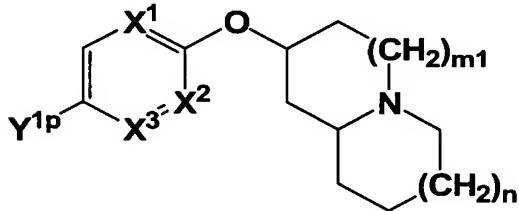


[wherein L_2 and Y^{1p} have the same meanings as above] in the presence of a catalyst to give a compound of a general formula (XII):



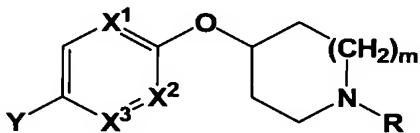
(XII)

5 (wherein X^1 , X^2 , X^3 , m , R^1 and Y^{1p} have the same meanings as above), or a compound of a general formula (XIII):



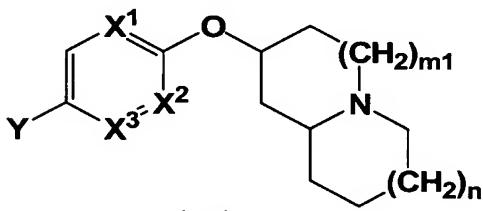
(XIII)

(wherein X^1 , X^2 , X^3 , $m1$, n and Y^{1p} have the same meanings as above), and optionally the protective group is removed to give a compound of a general formula (I-2):



(I-2)

10 [wherein X^1 , X^2 , X^3 , m , R and Y have the same meanings as above], or a compound of a general formula (I-3):



(I-3)

[wherein X^1 , X^2 , X^3 , $m1$, n and Y have the same meanings as above].

15 Regarding the reaction of the compound of formula (IX) with the compound of formula (X), in general, from 0.5 mols to 5 mols, preferably from 0.7 mols to 3 mols of a compound (X) is reacted with 1 mol of a compound (IX).

The catalyst to be used in the reaction may be a transition metal generally used in cross-coupling reaction, such as copper, nickel, palladium. More concretely, preferred are tetrakis (triphenylphosphine)palladium(0), palladium(II) acetate, bis(triphenylphosphine)palladium(II) chloride,

[1,1'-bis(diphenylphosphino)ferrocene]palladium(II) dichloride.

The reaction is effected generally in an inert solvent. The inert solvent is, for example, preferably water, benzene, toluene, xylene, methylene chloride, chloroform, dimethoxyethane, tetrahydrofuran, dioxane, dimethylformamide, and their mixed solvents.

5 The reaction temperature may be generally from room temperature to the boiling point of the solvent used in the reaction, preferably from 20°C to 200°C.

The reaction time may be generally from 30 minutes to 7 days, preferably from 3 hours to 2 days.

10 Preferably, the reaction is effected in the presence of a base. The base includes, for example, an inorganic base such as sodium hydroxide, potassium hydroxide, sodium hydrogencarbonate, sodium carbonate, potassium carbonate, cesium carbonate; and an organic base such as triethylamine, diisopropylamine.

The amount of the base to be used may be generally from 0.5 mols to 5 mols, preferably from 0.7 mols to 3 mols relative to 1 mol of the compound of formula (IX).

15 After the reaction, when the reaction product has a protective group, then the protective group is removed, but when the reaction product does not have a protective group, then it may be directly processed in an ordinary manner to obtain a compound of the invention.

The removal of the protective group and the post-treatment of the reaction product may be effected according to the methods described hereinabove in the section or Production Method 1.

20 The compound of formula (X) may be prepared in any known methods or according to such known methods, or according to the methods described in Examples and Reference Examples given hereinunder, optionally suitably combining any of such methods.

The compound of formula (X) may be produced according to the following reaction:

1) Reaction of a compound of formula (VI) with a lower alkyl metal;

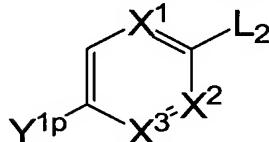
25 2) Reaction of a compound of formula (VI) with a lower alkyl metal followed by further reaction with a metal halide or an ester, or

3) Reaction of a compound of formula (VI) with a bis(tri-lower alkyl-tin) or bis(borate) in the presence of a catalyst.

The compounds of the invention may also be produced according to the following method.

30 Production Method 3

A compound of a general formula (XIV):

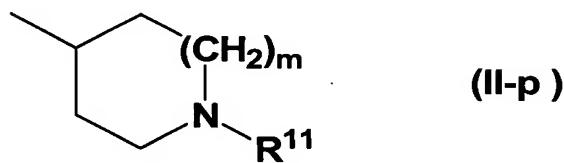


(XIV)

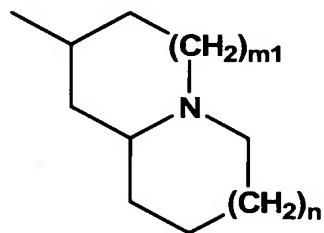
[wherein the symbols have the same meanings as above] is reacted with a compound of a general formula (XV):

W¹—OH (XV)

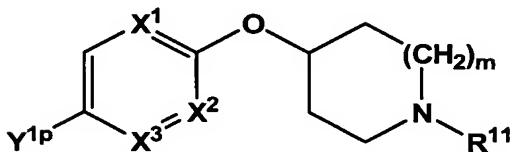
[wherein W¹ represents a group of the following formula (II-p):



(wherein R¹¹ is R¹ or an amino-protective group; and the other symbols have the same meanings as above), or represents a group of a formula (III):

**(III)**

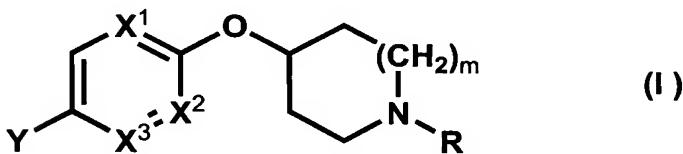
(wherein the symbols have the same meanings as above)] or its salt to give a compound of a general formula (XVI):

**(XVI)**

10 [wherein X¹, X², X³, Y^{1p}, m and R¹¹ have the same meanings as above], and when the compound and R¹¹ have a protective group for the amino group therein, then the amino-protective group is removed, and thereafter this is further reacted with a precursor aldehyde or ketone corresponding to R¹ or with a compound of a general formula (XVII):

R¹—L₂ (XVII)

15 [wherein the symbols have the same meanings as above], and optionally the protective group is removed to give a compound (I) of the invention:



(wherein the symbols have the same meanings as above).

20 The compounds of formulae (I), (I-2) and (I-3) of the invention may be readily isolated and purified in any ordinary separation methods. Examples of the methods include solvent extraction,

recrystallization, reprecipitation, column chromatography, thin-layer partitioning chromatography.

The compounds may be converted into pharmaceutically-acceptable salts or esters in an ordinary manner. On the contrary, their salts or esters may be converted into free compounds also in an ordinary manner.

5 The heteroaryloxy-nitrogen-containing saturated heterocyclic derivatives of the invention may be in the form of their pharmaceutically-acceptable salts, and the compounds of formula (I) may be produced in any ordinary manner. The acid-addition salts of the compounds includes, for example, hydrohalides such as hydrochlorides, hydrofluorides, hydrobromides, hydroiodides; inorganic acid salts such as nitrates, perchlorates, sulfates, phosphates, carbonates; lower alkylsulfonates such as 10 methanesulfonates, trifluoromethanesulfonates, ethanesulfonates; arylsulfonates such as benzenesulfonates, p-toluenesulfonates; organic acid salts such as fumarates, succinates, citrates, tartrates, oxalates, maleates; and other acid-addition salts with organic acids such as amino acids, for example, glutamates, aspartates.

15 The salts may also be base-addition salts, for example, salts with alkali metals such as sodium potassium; salts with alkaline earth metals such as calcium, magnesium; ammonium salts; salts with organic bases such as guanidine, triethylamine, dicyclohexylamine. Further, the compounds of the invention may also be in the form of hydrates or solvates of their free compounds or salts.

20 The usefulness of the compounds of formula (I) of the invention as medicines is proven, for example, by the following pharmaceutical test examples.

20 Pharmaceutical Test Example 1 (histamine analogue-binding inhibition test)

A cDNA sequence coding for a human histamine-3 receptor [see International Patent Application WO00/39164) was cloned with expression vectors pCR2.1, pEF1x (by Invitrogen) and pCI-neo (by Promega). The resulting expression vector was transfected into host cells, HEK293 and CHO-K1 (American Type Culture Collection), according to a cationic lipid process [see *Proceedings of the National Academy of Sciences of the United States of America*, Vol., 84, p. 7413 (1987)] to obtain histamine-3 receptor expression cells.

30 A membrane specimen prepared from the cells having expressed a histamine-3 receptor was incubated in an assay buffer (50 mM Tris buffer, pH 7.4) along with a test compound and 20,000 cpm of [³H]- α -methylhistamine (by NEN) therein at 25°C for 2 hours, and then filtered through a glass filter GF/C. This was washed with 50 mM Tris buffer (ph 7.4), and the radioactivity on the glass filter was measured. The non-specific binding was determined in the presence of 10 μ M thioperamide (by SIGAM), and the 50 % inhibitory concentration (IC₅₀) of the test compound to specific N- α -methylhistamine binding was calculated [see *Molecular Pharmacology*, Vol. 55, p. 1101 (1999)]. As a result, IC₅₀ of the compound of Example 1 was 15 nM.

35 As in the above, the compounds of the invention strongly inhibited the binding of the histamine-3 receptor to N- α -methylhistamine (histamine analogue).

Pharmaceutical Test Example 2 (antagonistic test to drinking behavior induced by histamine-3 receptor selective agonist, R- α -methylhistamine)

While anesthetized with ketamine-xylazine (74 and 11 mg/kg, single intraabdominal

administration), a chronic guide cannula (26 gauge, length 11 mm) was inserted into the third ventricle of male SD rats (7 to 10-weeks age, 200 to 300 g), using a brain stereotaxis device, and fixed with a dental resin. The position of the tip of the guide cannula was 2.2 mm after the bregma, on the median line and at a depth of 8 mm from the surface of the cranial bone. After the recovery period of about 1 week, 5 R- α -methylhistamine (0.3 μ g/1 μ L/head, 30 % propylene glycol solution) was administered into the third ventricle. A test compound suspended in an aqueous 0.5 % methyl cellulose solution was orally administered to the rats 2 hours before the administration of R- α -methylhistamine thereto, and the amount of water drunk by the rats 1 hour after the administration of R- α -methylhistamine was determined.

10 As a result, the compound of the invention administered to the rats in an amount of 10 mg/kg significantly inhibited the increase in the amount of water drunk by the rats with R- α -methylhistamine administered to the third ventricle thereof.

Pharmaceutical Test Example 3 (test for internal kinetics)

15 A test compound was orally or intravenously administered to SD male rats (7 to 10 weeks-age, 200 to 400 g) kept away from eating and drinking overnight, and using a heparinization capillary within a predetermined period of time, about 100 μ l of the blood was collected from them via their tail vein. The blood was centrifuged (4°C, 6000 rpm, 10 minutes) to collect its plasma. Ethanol (including an internal standard substance) was added to the plasma in an amount of 3 times that of the plasma, and stirred, and left statically at -20°C for 20 minutes, and then this was centrifuged (4°C, 10,000 rpm, 10 minutes). The 20 supernatant was analyzed through LC/MS/MS, and the plasma concentration of the compound was quantified according to a relative calibration curve method.

As a result, the bioavailability of the compound of Example 1 was 53 %, and the half-value period in blood thereof was 5.3 hours.

Pharmaceutical Test Example 4 (brain/cerebrospinal fluid migration test)

25 A test compound was orally or intravenously administered to SD male rats (7 to 10 weeks-age, 200 to 400 g), and while anesthetized with ether for a predetermined period of time, the whole blood was collected from the abdominal aorta of the rats, using a heparin-processed syringe. Next, the brain skin was cut opened and a 30 G needle for dental use was pierced between the cervical vertebrae and inserted into the subarachnoid cavity. Through the tube connected with the dental 30 G needle, from 50 to 100 30 μ l of the cerebrospinal fluid was collected into a 1-ml syringe, and then the brain was taken out. The blood sample was centrifuged (4°C, 6000 rpm, 10 minutes), and the resulting plasma was stirred with ethanol (including an internal standard substance) added thereto in an amount of 3 times the plasma. 2 ml of water was added to the brain sample and homogenized, and a part of the resulting mixture was stirred with ethanol (including an internal standard substance) added thereto in an amount of 3 times the mixture. 35 These samples were kept at -20°C for 20 minutes, and then centrifuged (4°C, 12,000 g, 10 minutes), and the resulting supernatant was analyzed through LC/MS/MS. According to a relative calibration curve method, the concentration of the test compound in the plasma, the brain and the cerebrospinal fluid was quantified.

As a result, 2 hours after the oral administration (10 mg/kg) thereof, the brain concentration of

the compound of Example 1 was 6.18 nmol/g, the cerebrospinal fluid concentration thereof was 0.128 μ M, and the plasma concentration thereof was 0.54 μ M.

The compounds of formula (I) may be administered orally or parenterally, and may be formulated into pharmaceutical preparations suitable to such administration modes. Using them, the invention provides preventives and remedies for metabolic system diseases such as obesity, diabetes, hormone secretion disorder, hyperlipemia, gout, fatty liver; circulatory system diseases, for example, stenocardia, acute/congestive cardiac insufficiency, cardiac infarction, coronary arteriosclerosis, hypertension, nephropathy, and central and peripheral nervous system diseases such as bulimia, emotional disorder, melancholia, anxiety, epilepsy, delirium, dementia, schizophrenia, attention deficit/hyperactivity disorder, memory disorder, Alzheimer's disease, Parkinson's disease, sleep disorder, recognition disorder, motion disorder, paresthesia, dysosmia, epilepsy, morphine resistance, narcotic dependency, alcoholic dependency.

In clinical use of the compounds of the invention, pharmaceutically-acceptable additives may be added thereto to formulate various preparations in accordance with the intended administration route thereof, and the preparations may be administered. Various additives generally used in the field of pharmaceutical compositions may be used herein, including, for example, gelatin, lactose, white sugar, titanium oxide, starch, crystalline cellulose, hydroxypropylmethyl cellulose, carboxymethyl cellulose, corn starch, microcrystalline wax, white petrolatum, magnesium metasilicate aluminate, anhydrous calcium phosphate, citric acid, trisodium citrate, hydroxypropyl cellulose, sorbitol, sorbitan fatty acid ester, polysorbate, sucrose fatty acid ester, polyoxyethylene, hardened castor oil, polyvinylpyrrolidone, magnesium stearate, light silicic acid anhydride, talc, vegetable oil, benzyl alcohol, gum arabic, propylene glycol, polyalkylene glycol, cyclodextrin, and hydroxypropylcyclodextrin.

Combined with such additives, the compound of the invention may be formulated into various forms of preparations, for example, solid preparations such as tablets, capsules, granules, powders and suppositories; and liquid preparations such as syrups, elixirs and injections. These preparations can be produced in any method known in the field of pharmaceutical compositions. The liquid preparations may be in such a form that is dissolved or suspended in water or in any other suitable medium before use. Especially for injections, the preparation may be dissolved or suspended, if desired, in a physiological saline or glucose solution, and a buffer and a preservative may be added thereto.

The preparations may contain the compound of the invention in an amount of from 1.0 to 100 % by weight, preferably from 1.0 to 60 % by weight of the preparation. The preparations may contain any other therapeutically-effective compound.

In their use, the compounds of the invention may be combined with any other agents useful for treatment of metabolic disorders and/or dietary disorders. The individual ingredients to be combined may be administered at the same time or at different times during the treatment period, either as one preparation or as divided different preparations. Accordingly, the invention should be so interpreted that it encompasses any and every administration mode at the same time or at different times, and the administration in the invention should be interpreted so. The range of the combination of the compound of the invention and the other agent useful for treatment of metabolic disorders and/or dietary disorders

encompasses, in principle, all combinations of the compound of the invention and any and every agent useful for the treatment of metabolic disorders and/or dietary disorders.

The compound of the invention may be used, as combined with a pharmaceutical agent effective for hypertension, obesity-related hypertension, hypertension-related disorders, cardiomegaly, left 5 ventricle hypertrophy, metabolic disorders, obesity, obesity-related disorders (the agent is hereinafter referred to as co-agent). In prevention and treatment of the above-mentioned diseases, the pharmaceutical agents may be administered simultaneously or separately or successively. When the compound of the invention is used along with one or more such co-agents, then they may be formulated into one pharmaceutical composition for single administration. In combination therapy, however, a 10 composition containing the compound of the invention and a co-agent may be separately formulated in different packages, and they may be administered simultaneously or separately or successively. They may be administered at different times.

The dose of the co-agent may depend on the clinical use thereof, and may be suitably determined in accordance with the administration object, the administration route, the diseases and the 15 combination. The form of the co-agent for administration is not specifically defined, and it may be combined with the compound of the invention when they are administered. The administration mode includes, for example, the following: (1) A compound of the invention is combined with a co-agent to give a single preparation for single administration; (2) a compound of the invention and a co-agent are separately formulated into different two preparations, and the two preparations are simultaneously 20 administered in one administration route; (3) a compound of the invention and a co-agent are separately formulated into different two preparations, and they are administered at different times in one and the same administration route; (4) a compound of the invention and a co-agent are separately formulated into different two preparations, and they are administered at the same time in two different administration routes; (5) a compound of the invention and a co-agent are separately formulated into different two 25 preparations, and they are administered at different times in different administration routes (for example, a compound of the invention and a co-agent are administered in that order, or in an order contrary to this). The blend ratio of the compound of the invention and the co-agent may be suitably determined depending on the administration object, the administration route, and the disease for the administration.

The co-agent for use in the invention includes, for example, "therapeutical medicines for 30 diabetes", "therapeutical medicines for hyperlipemia", "therapeutical medicines for hypertension", and "anti-obesity medicines". Two or more these co-agents may be used, as combined in any desired ratio.

The "therapeutical medicines for diabetes" include, for example 1) PPAR- γ agonists such as 35 glitazones [e.g., ciglitazone, darglitazone, englitazone, isoglitazone, MCC-555], pioglitazone, rosiglitazone, troglitazone, BRL49653, CLX-0921, 5-BTZD, GW-0207, LG-100641, LY-300512; 2) biguanides such as metformin, buformin, phenformin; 3) protein tyrosine phosphatase 1B inhibitors; 4) sulfonylureas such as acetohexamide, chloropropamide, diabinese, glibenclamide, glipizide, glyburide, glimepiride, glicilazide, glipentide, gliquidone, glisolamide, trazamide, tolbutamide; 5) meglitinides such as repaglinide, nateglinide; 6) α -glucoside hydrolase inhibitors such as acarbose, adiposine, camiglibose, emiglitate, miglitol, voglibose, pradimicin-Q, salbostatin, CKD-711, MDL-25,673,

MDL-73,945, MOR14; α -amylase inhibitors such as tendamistat, trestatin, A13688; 8) insulin secretion promoters such as linoglitride, A-4166; 9) fatty acid oxidation inhibitors such as clomoxir, etomoxir; 10) A2 antagonists such as midaglizole, isaglidole, deriglidole, idazoxan, earoxan, fluparoxan; 11) insulin or insulin mimetics such as biota, LP-100, novalapid, insulin detemir, insulin lispro, insulin glargine, insulin zinc, Lys-Pro-insulin, GLP-1 (73-7), GLP1 amide (7-36); 12) non-thiazolidinedione such as JT-501 and farglitazar; 13) PPAR α/γ co-agonists such as CLX-0940, GW-1536, GW-1929, GW-2433, KPR-297, L-796449, L-90, SB219994.

The "therapeutic medicines for hyperlipidemia" include, for example 1) bile acid absorption promoters such as cholesterylamine, colestevole, colestipol, crosslinked dextran dialkylaminoalkyl derivatives, Colestid®, LoCholest®, Questran®; 2) HMG-CoA reductase inhibitors such as atorvastatin, itavastatin, fluvastatin, lovastatin, pravastatin, rivastatin, rosuvastatin, simvastatin, ZD-4522; 3) HMG-CoA synthase inhibitors; 4) cholesterol absorption inhibitors such as snatol ester, β -sitosterol, sterol glucoside, ezetimibe; 5) acyl-coenzyme A cholesterol acyltransferase inhibitors such as avasimibe, eflucimibe, KY-505, SMP-709; 6) CETP inhibitors such as JTT705, torcetrapib, CP532632, BAY-63-2149, SC-591, SC-795; 7) squalane synthesis inhibitors; 8) antioxidants such as probucol; 9) PPAR α agonists such as beclofibrate, benzafibrate, syprofibrate, clofibrate, etofibrate, fenofibrate, gemcabene, gemfibrozil, GW-7647, BM-170744, LY-518674, fibrin acid derivatives (e.g., Atromid®, Lopid®, Tricor®); 10) FXR receptor antagonists such as GW-4064, SR-103912; 11) LXR receptor agonists such as GW3965, T9013137, XTCO-179628; 12) lipoprotein synthesis inhibitors such as niacin; 13) renin-angiotensin system inhibitors; 14) microsome triglyceride transportation inhibitors; 15) bile acid reabsorption inhibitors such as BARA1453, SC435, PHA384640, S-435, AZD7706; 16) PPAR δ agonists such as GW501516, GW590735; 17) triglyceride synthesis inhibitors; 18) MTTP inhibitors such as LAB687, CP346086; 19) low-density lipoprotein; 20) squalane epoxidase inhibitors; 21) platelet agglutination inhibitors; 22) 5-lipoxygenase activation protein inhibitors such as MK-591.

The "therapeutic medicines for hypertension" include, for example 1) diuretics such as thiazide diuretics such as chlorothialidon, chlorothiazide, dichlorofenamide, hydrofluorothiazide, indapamide, hydrochlorothiazide; loop diuretics such as bumetanide, ethacrynic acid, furosemide, tolusemide; sodium diuretics such as amiloride, triamterene; aldosterone antagonist diuretics such as spironolactone, epilenone; 2) β -adrenaline blockers such as acebutolol, atenolol, betaxolol, bevantolol, bisoprolol, bopindolol, carteolol, carvedilol, celiprolol, esmolol, indeolol, metaprolol, nadolol, nebivolol, penbutolol, pindolol, propanolol, sotalol, tartatolol, tilisolol, timolol; 3) calcium channel blockers such as amlodipine, aranidipine, azelnidipine, barnidipine, benidipine, bepridil, cinaldipine, clevidipine, diltiazem, efonidipine, felodipine, gallopamil, isradipine, lacidipine, lemidipine, lercanidipine, nicardipine, nifedipine, nilvadipine, nimodepine, nisoldipine, nitrendipine, manidipine, pranidipine, verapamil; 4) angiotensin transferase inhibitors such as benazepril, captopril, cilazapril, delapril, enalapril, fosinopril, imidapril, rosinopril, moexipril, quinapril, quinapril, ramipril, perindopril, perindopril, quanipril, spirapril, tenocapril, transolapril, zofenopril; 5) neutral endopeptidase inhibitors such as omapatrilat, cadoxatril, ecadotril, fosidotril, sampatrilat, AVE7688, ER4030; 6) endoserine antagonists such as tezosentan, A308165, YM62899; 7) vasodilators such as hydralazine, clonidine, minoxidil, nicotinyl

alcohol; 8) angiotensin II antagonists such as candesartan, eporsartan, iribesartan, rosartan, pratosartan, tasosartan, telmisartan, balsartan, EXP-3137, FI6828K, RNH6270; 9) α/β adrenalin blockers such as nipradiol, arotinolol, amoslalol; 10) α_1 blockers such as terazosin, urapidil, purazosin, bunazosin, trimazosin, doxazosin, naphthopidil, indolamin, WHIP164, XEN010; 11) α_2 agonists such as lofexidine, 5 tiamenidine, moxonidine, rilmenidine, guanobenz; 12) aldosterone inhibitors.

The "anti-obesity medicines" include, for example 1) 5HT (serotonin) transporter inhibitors such as paraxetin, fluoxetine, fenfluramine, fluvoxamine, sertraline, imipulamin; 2) norepinephrine transporter inhibitors such as GW320659, decipulamin, talsupram, nomifensin; 3) cannabinoid-1 receptor 10 1 (CB-1) antabonists/inverse-agonists such as limonabant (Sanofi Synthelabo), SR-147778 (Sanofi Synthelabo), BAY-65-2520 (Bayer), SLV-319 (Sorbei), as well as compounds disclosed in USP 5,532,237, USP 4,973,587, USP 5,013,837, USP 5,081,122, USP 5,112,820, USP 5,292,736, USP 5,624,941, USP 6,028,084, WO96/33159, WO98/33765, WO98/43636, WO98/43635, WO01/09120, WO01/96330, WO98/31227, WO98/41519, WO98/370621, WO00/10967, WO00/10968, WO97/29079, WO99/02499, WO01/58869, WO02/076949, WO01/64632, WO01/64633, WO01/64634, WO03/006007, WO03/007887, EP-658546; 4) glerin antagonists such as compounds disclosed in WO01/87355, WO02/08250; 5) histamine(H3) antagonists/inverse-agonists such as thioperamide, 3-(1H-imidazol-4-yl)propyl-N-(pentenyl)carbonate, clobenpropit, iodofenpropit, imoproxyfen, GT2395, A331440, compounds disclosed in WO02/15905, O-[3-(1H-imidazo-4-yl)propanol] carbamate, piperazine-containing H3-receptor antagonists (Lazewska, D. et al., *Phrmazie*, 56: 927-32 (2001), benzophenone derivatives Sasse, A. et al., *Arch. Pharm.* (Weinheim) 334: 45-52 (2001)), substituted 20 N-phenylcarbamates (Reidemeister, S. et al., *Pharmazie*, 55: 83-6 (2000)), proxyfen derivatives (Sasse, A. et al., *J. Med. Chem.*, 43: 3335-43 (2000)); 6) MCH-1R antagonists such as T-226296 (Takeda), SNP-7941 (Synaptic), other compounds disclosed in WO01/82925, WO01/87834, WO02/051809, WO02/06245, WO02/076929, WO02/076947, WO02/04433, WO02/51809, WO02/083134, WO02/094799, WO03/004027, JP-A-2001-226269; 7) MCH-2R agonists/antagonists; 8) NPY1 25 antagonists such as isopropyl 3-chloro-5-(1-(6-[2-(5-ethyl-4-methyl-thiazol-2-yl)ethyl]-4-morpholinyl-4-yl-pyridin-2-ylamino)-ethyl)p henyl]carbamate, BIBP3226, BIBO3304, LY-357897, CP-671906, GI-264879, and other compounds disclosed in USP 6,001,836, WO96/14307, WO01/23387, WO99/51600, WO01/85690, WO01/85098, WO01/85173, WO01/89528; 9) NPY5 antagonists such as 152804, GW-569180A, GW-594884A, GW-587081X, GW-548118X, FR235,208, FR226928, FR240662, FR252384, 1229U91, GI-264879A, CGP71683A, LY-377897, LY366377, PD-160170, SR-120526A, SR-120819A, JCF-104, H409/22, and other compounds disclosed in USP 6,140,354, USP 6,191,160, USP 6,258,837, USP 6,313,298, USP 6,337,332, USP 6,329,395, USP 340,683, USP 6,326,375, USP 6,329,395, USP 6,337,332, USP 6,335,345, EP-01010691, EP-01044970, WO97/19682, WO97/20820, WO97/20821, WO97/20822, WO97/20823, WO98/27063, WO00/107409, WO00/185714, WO00/185730, WO00/64880, WO00/68197, WO00/69849, WO01/09120, WO01/14376, WO01/85714, WO01/85730, WO01/07409, WO01/02379, WO01/02379, WO01/23388, WO01/23389, WO01/44201, WO01/62737, WO01/62738, WO01/09120, WO02/20488, WO02/22592, WO02/48152, WO02/49648, WO02/094789, and compounds disclosed in

Norman et al., *J. Med. Chem.*, 43: 4288-4312 (2000); 10) leptins such as human recombinant leptin (PEG-OB, Hoffman La Roche), recombinant methionylleptin (Amgen); 11) leptin derivatives such as compounds disclosed in USP 5,552,524, USP 5,552,523, USP 5,552,522, USP 5,521,283, WO96/23513, WO96/23514, WO96/23515, WO96/23516, WO96/23517, WO96/23518, WO96/23519, WO96/23520;

5 12) opioid antagonists such as narmefen (Revex®), 3-methoxynartorexon, naroquison, nartoxon, compounds disclosed in WO00/21509; 13) aurexin antagonists such as SB-334867A, and other compounds disclosed in WO01/96302, WO01/68609, WO02/51232, WO02/51838, and WO03/023561; 14) bombesin receptor subtype-3 agonists; 15) cholecistokinin A (CCK-A) agonists such as AR-R15849, GI-181771, JMV-180, A-71378, A-71623, SR-146131, compounds described in USP 5,739,106; 16) 10 CNTF (ciliary neurotrophic factors) such as GI-181771 (Glaxo-Smith Kline), SR146131 (Sanofi Synthelabo), butabindide, PD170,292, PS149164 (Pfizer); 17) CNTF derivatives such as axokine (Regeneron), and other compounds disclosed in WO94/09134, WO98/22128, WO99/43813; 18) growth hormone secretion receptor agonists such as NN703, hexarelin, MK-0677, SM-130686, CO-424,391, L-692,429, L-163,255, and compounds disclosed in USP 6,358,951, US Patent Application Nos. 15 2002/049196, 2002/022637, WO01/56592, WO02/32888; 19) serotonin receptor-2C agonists such as BVT933, DPCA37215, IK264, PNU22394, WAY161503, R-1065, YM348, and other compounds disclosed in USP 3,914,250, WO02/36596, WO02/48124, WO02/10169, WO01/66548, WO02/44152, WO02/51844, WO02/40456, WO02/40457; 20) melanocholtin-3 receptor agonists; 21) melanocholtin-4 receptor agonists such as CHIR86036 (Chiron), ME-10142, ME-10145 (Melacure), and other compounds 20 disclosed in WO99/64002, WO00/74679, WO01/991752, WO01/74844, WO01/70708, WO01/70337, WO01/91752, WO02/059095, WO02/059107, WO02/059108, WO02/059117, WO02/12166, WO02/11715, WO02/12178, WO02/15909, WO02/068387, WO02/068388, WO02/067869, WO03/007949, WO03/009847; 22) monoamine reabsorption inhibitors such as cibtramin (Meridia®/Recuctil®) and its salts, and other derivatives disclosed in USP 4,746,680, USP 4,806,570, 25 USP 5,436,272, US Patent Application No. 2002/0006964, WO01/27068, WO01/62341; 23) serotonin re-uptake inhibitors such as dextroamphetamine, fluoxetine, and other compounds disclosed in USP 6,365,633, WO01/27060, WO01/162341; 24) glucagon-like peptide-1 agonists; 25) topiramate (Topimax®); 26) phytopharm compound 57 (e.g., CP644,673); 27) acetyl CoA carboxylase-2 (ACC2) inhibitors; 28) β-adrenalin receptor-3 agonists such as AD9677/TAK677 (Dai-Nippon 30 Pharmaceutical/Takeda Chemical), CL-316,243, SB418790, BRL-37344, L-796568, BMS-196085, BRL-35135A, CGP12177A, BTA-243, W427353, trecadrine, Zeneca D7114, SR59119A, and other compounds disclosed in USP 5,705,515, USP 5,451,677, WO01/74782, WO02/32897; 29) diacylglycerol acyltransferase-1 inhibitors; 30) diacylglycerol acyltransferase-2 inhibitors, 31) fatty acid synthesis inhibitors such as carulenin, C75; 32) phosphodiesterase inhibitors such as theophylline, pentoxifylline, 35 zaprinast, sildenafil, amrinone, milrinone, cilostamide, rolipram, cilomilast; 32) thyroid hormone-β agonists such as KB-2611 (KaroBioBMS), and other compounds disclosed in WO02/15845, JP-A 2000-256190; 33) phytanic acids such as phytanic acid, 4-[(E)-2-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl-1-propenyl]benzoic acid (TTNPB), retinoic acid, and other compounds disclosed in WO99/00123; 34) acylestrogens such as oleoylestrone,

and other compounds disclosed in del Mar-Grasa, M. et al., *Obesity Research*, 9:202-9 (2001); 35) glucocorticoid antagonists; 36) 11- β hydroxysteroid dehydrogenase-1 inhibitors such as BVT3498, BVT2733, and other compounds disclosed in WO01/90091, WO01/90090, WO01/90092; 37) stearoyl-CoA desaturase-1 inhibitors; 38) dipeptidyl peptidase-IV inhibitors such as isoleucine 5 thiazolidine, valine pyrrolidine, NVP-DPP728, AF237, P93/01, TSL225, TMC-2A/2B/2C, FE999011, P9310/K364, VIP0177, SDZ274-444, and other compounds disclosed in WO03/004498, WO03/004496, EP1258476, WO02/083128, WO02/062764, WO03/000250, WO03/002530, WO03/002531, WO03/002553, WO03/002593, WO03/000180, WO03/000181; 39) lipase inhibitors such as tetrahydrolitatin (Orlistat/Xenical®), Triton WR1339, RHC80267, lipstatin, teasaponin, 10 diethylumbelliferyl phosphate, FL-386, WAY-121898, Bay-N-3176, valilactone, esteracin, evelactone A, evelactone B, RHC80267, and other compounds disclosed in WO01/77094, USP 4,598,089, USP 4,452,813, USP 5,512,565, USP 5,391,571, USP 5,602,151, USP 4,405,644, USP 4,189,438, USP 4,242,453; 39) fatty acid transporter inhibitors; 40) dicarboxylate transporter inhibitors; 41) glucose transporter inhibitors; 42) phosphate transporter inhibitors.

15 The combined pharmaceutical agents may be obtained by combining a compound of the invention and one or more of the above-mentioned co-agents. The combined pharmaceutical agents are useful for prevention and treatment of metabolic disorders, when combined with one or more medicines selected from a group consisting of medicines of diabetes and medicines for hyperlipemia. In particular, the combined pharmaceutical agents that comprise a medicine for hypertension and an anti-obesity 20 medicine and contain a medicine for diabetes and/or a medicine for hyperlipemia added thereto are useful for prevention and treatment of metabolic disorders owing to the synergistic effects of the ingredients therein.

25 When the compounds of the invention are used in clinical sites, then the dose and the administration frequency thereof may vary depending on the sex, the age, the body weight and the condition of the patient and on the type and the scope of the treatment of the patient. In oral administration, in general, the dose may be from 0.01 to 100 mg/kg-adult/day, preferably from 0.03 to 1 mg/kg-adult/day, and it may be administered all at a time or may be administered in a few times as divided into a few portions. In parenteral administration, its dose may be from 0.001 to 10 mg/kg-adult/day, preferably from 0.001 to 0.1 mg/kg-adult/day, and it may be administered all at a time 30 or may be administered in a few times as divided into a few portions.

Any ordinary physicians, veterinarians and clinicians may readily determine the effective dose necessary for retarding, inhibiting or stopping the disease development, and may suitably treat patients.
example

35 The invention is described more concretely with reference to Examples and Reference Examples mentioned below, which, however, do not restrict the invention.

Formulation Example 1:

10 parts of the compound of Production Example 1, 15 parts by weight of heavy magnesium oxide and 75 parts by weight of lactose were uniformly mixed to prepare a powdery or granular preparation having a particle size of at most 350 μ m. The preparation was encapsulated to give

capsules.

Formulation Example 2:

45 parts of the compound of Production Example 1, 15 parts of starch, 16 parts of lactose, 21 parts of crystalline cellulose, 3 parts of polyvinyl alcohol and 30 parts of distilled water were uniformly mixed, then ground, granulated and dried, and then sieved to give a granular preparation having a particle diameter of from 1410 to 177 μm .

Formulation Example 3:

A granular preparation was prepared in the same manner as in Formulation Example 2. 96 parts of the granular preparation was mixed with 3 parts of calcium stearate, and shaped under compression into tablets having a diameter of 10 mm.

Formulation Example 4:

90 parts of the granular preparation obtained according to the method of Formulation Example 2 was mixed with 10 parts of crystalline cellulose and 3 parts of calcium stearate, and shaped under compression into tablets having a diameter of 8 mm. These were coated with a mixed suspension of syrup gelatin and precipitated calcium carbonate to give sugar-coated tablets.

For thin-layer chromatography in Examples, used was a plate of Silicagel 60F₂₄₅ (Merck); and for detection, used was a UV detector. Wakogel C-300 (Wako Pure Chemicals) was used for the column silica gel; and LC-SORB SP-B-ODS (Chemco) or YMC-GEL ODS-AQ 120-S50 (Yamamura Chemical Laboratories) was for the reversed-phase column silica gel. Mass spectrum was determined according to an electrospray ionization (ESI) process, using QuattroII (Micromass).

Abbreviations in Examples have the following meanings.

i-Bu: isobutyl group

n-Bu: n-butyl group

t-Bu: t-butyl group

Me: methyl group

Et: ethyl group

Ph: phenyl group

i-Pr: isopropyl group

n-Pr: n-propyl group

CDCl₃: heavy chloroform

CD₃OD: heavy methanol

DMSO-d₆: heavy dimethylsulfoxide

Abbreviations in nuclear magnetic resonance spectrum have the following meanings:

s: singlet

d: doublet

dd: double doublet

t: triplet

m: multiplet

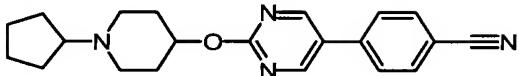
br: broad

q: quartet

J: coupling constant

Hz: hertz

Example 1:



2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-cyanophenyl) pyrimidine

1) Production of 2-(1-t-butoxycarbonylpiperidin-4-yloxy)-5-bromopyrimidine:

10 1-t-butoxycarbonyl-4-hydroxypiperidine (408 mg, 2.03 mmol) and cesium carbonate (764 mg, 2.34 mmol) were added to a DMF solution (10 ml) of 2-chloro-5-bromopyrimidine (300 mg, 1.56 mmol), and stirred at room temperature for 14 hours. Water was added to the reaction mixture, and extracted with ethyl acetate. The organic layer was washed with saturated saline, dried with anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified through silica gel column chromatography (C-300, hexane:ethyl acetate = 10:1) to obtain the entitled compound (268 mg, 48 %).

15 2) Production of 2-(1-t-butoxycarbonylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine:

20 2-dimethoxyethane (2.0 ml) and aqueous 2 N sodium carbonate solution (0.7 ml) were added to 2-(1-t-butoxycarbonylpiperidin-4-yloxy)-5-bromopyrimidine (149 mg, 0.42 mmol), and then 4-cyanoboric acid (75.2 mg, 0.51 mmol) and tetrakis(triphenylphosphine)palladium(0) (10 mg, 0.0087 mmol) were added thereto and stirred in a nitrogen atmosphere at 90°C for 3 hours. The reaction mixture was cooled to room temperature, and extracted with ethyl acetate. The organic layer was washed with saturated saline, dried with anhydrous sodium sulfate and concentrated under reduced pressure. The residue was purified through silica gel column chromatography (C-300, hexane:ethyl acetate = 3:1) to obtain the entitled compound (122 mg, 77 %).

25 3) Production of 2-(piperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine:

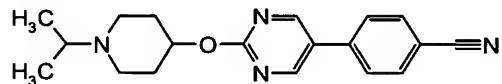
30 Trifluoroacetic acid (1.5 ml) was added to a methylene chloride solution (2.0 ml) of 2-(1-t-butoxycarbonylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine (122 mg, 0.32 mmol) at room temperature, and stirred for 2.5 hours at the temperature. The reaction solution was concentrated under reduced pressure, and the residue was extracted with chloroform. The organic layer was washed with aqueous saturated sodium bicarbonate solution and saturated saline solution in that order, dried with anhydrous sodium sulfate, and concentrated under reduced pressure to obtain the entitled compound (90 mg, 100 %).

35 4) Cyclopentanone (0.022 mol) and 0.3 N zinc chloride-sodium borocyanide solution (0.55 ml) were added to a methanol solution (3.0 ml) of 2-(piperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine (46 mg, 0.16 mmol), and stirred at room temperature for 14 hours. The reaction mixture was concentrated under reduced pressure, and the residue was extracted with chloroform. The organic layer was washed with saturated saline solution, dried with anhydrous sodium sulfate, and concentrated under reduced pressure. The resulting residue was purified through partitioning thin-layer chromatography (chloroform:methanol = 10:1) to obtain the entitled compound (50 mg, 87 %).

¹HNMR (300 MHz, CDCl₃, δ ppm): 1.38-1.78 (6H, m), 1.82-2.04 (4H, m), 2.08-2.21 (2H, m), 2.32-2.63

(3H, m), 2.74-2.96 (2H, m), 5.07-5.18 (1H, m), 7.62 (2H, d, $J = 8.6$ Hz), 7.78 (1H, d, $J = 8.6$ Hz), 8.73 (2H, s); mass spectrum (ESI): 349 (M+H)

Example 2:

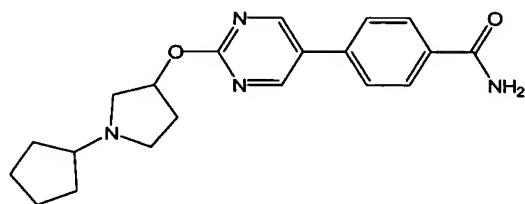


5 2-(1-isopropylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine

According to the same method as in Example 1, the entitled compound was obtained.

¹HNMR (300 MHz, CDCl₃, δ ppm): 1.10 (6H, d, $J = 6.5$ Hz), 1.88-2.05 (2H, m), 2.10-2.23 (2H, m), 2.43-2.60 (2H, m), 2.75-7.96 (3H, m), 5.08-5.20 (1H, m), 7.64 (2H, d, $J = 8.5$ Hz), 7.78 (2H, d, $J = 8.5$ Hz), 8.77 (2H, s); mass spectrum (ESI): 323 (M+H)

10 Example 3:



2-(1-cyclopentylpyrrolidin-3-yloxy)-5-(4-carbamoylphenyl)pyrimidine

1) Production of 2-(1-t-butoxycarbonylpiperidin-3-yloxy)-5-bromopyrimidine:

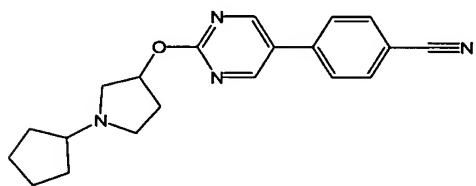
According to the same method as in Example 1-1) but using

15 1-t-butoxycarbonyl-3-hydroxypyrrolidine and 2-chloro-5-bromopyrimidine, the entitled compound was obtained.

2) According to the same method as in Example 1-2), 3) and 4) but using 2-(1-t-butoxycarbonylpiperidin-3-yloxy)-5-bromopyrimidine and 4-carbamoylphenylboronic acid, the entitled compound was obtained.

20 ¹HNMR (400 MHz, CDCl₃, δ ppm): 1.34-1.56 (4H, m), 1.57-1.67 (2H, m), 1.70-1.80 (2H, m), 1.82-1.92 (1H, m), 3.10-3.60 (6H, m), 5.35-5.42 (1H, m), 7.41 (1H, brs), 7.81 (2H, d, $J = 8.4$ Hz), 7.96 (2H, d, $J = 8.4$ Hz), 8.04 (1H, brs), 8.97 (2H, s); mass spectrum (ESI): 353 (M+H)

Example 4:

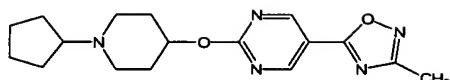


25 2-(1-cyclopentylpyrrolidin-3-yloxy)-5-(4-cyanophenyl)pyrimidine

According to the same method as in Example 3, the entitled compound was obtained.

¹HNMR (400 MHz, CDCl₃, δ ppm): 1.46-1.90 (8H, m), 2.03-2.13 (1H, m), 2.34-2.45 (1H, m), 2.52-2.65 (1H, m), 2.71-2.84 (3H, m), 3.22-3.34 (1H, m), 5.44-5.51 (1H, m), 7.62 (1H, d, $J = 8.4$ Hz), 7.76 (2H, d, $J = 8.4$ Hz), 8.71 (2H, s); mass spectrum (ESI): 335 (M+H)

30 Example 5:

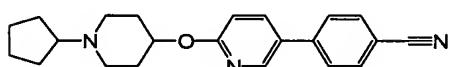


2-(1-cyclopentylpiperidin-4-yloxy)-5-[(4-methyl-1,3,5-oxadiazol-2-yl)phenyl]pyrimidine

According to the same method as in Example 1, the entitled compound was obtained.

¹HNMR (300 MHz, CDCl₃, δ ppm): 1.40-1.83 (6H, m), 1.83-2.25 (6H, m), 2.38-2.71 (3H, m), 2.50 (3H, s), 2.82-3.00 (2H, m), 5.12-5.30 (1H, m), 9.18 (2H, s); mass spectrum (ESI): 330 (M+H)

Example 6:



2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyridine

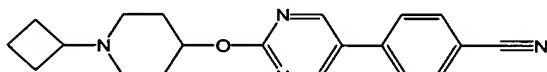
1) Production of 2-fluoro-5-[4-cyanophenyl]pyridine:

According to the same method as in Example 1-2) but using 2-fluoro-5-bromopyridine and 4-cyanophenylboronic acid, the entitled compound was obtained.

2) 60 % sodium hydride (13 mg) and 1-cyclopentyl-4-hydroxypiperidine (60 mg) were added to a DMF solution (3 ml) of 2-fluoro-5-[4-cyanophenyl]pyridine (56 mg), and stirred at 130°C for 7 hours. The reaction mixture was cooled to room temperature, and water was added thereto and extracted with ethyl acetate. The organic layer was washed with saturated saline solution, dried with anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was purified through silica gel column chromatography (C-300, chloroform:methanol = 9:1) to obtain the entitled compound.

¹HNMR (300 MHz, CDCl₃, δ ppm): 1.43-1.72 (6H, m), 1.81-1.92 (4H, m), 2.11-2.13 (2H, m), 2.44-2.66 (3H, m), 2.88-2.95 (2H, m), 5.12-5.19 (1H, m), 6.83 (1H, d J = 8.6 Hz), 7.62 (2H, d, J = 8.1 Hz), 7.72-7.81 (3H, m), 8.37 (1H, d, J = 1.9 Hz); mass spectrum (ESI): 348 (M+H)

Example 7:

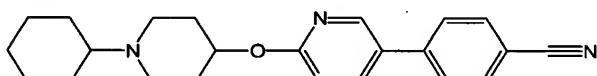


2-(1-cyclobutylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyridine

According to the same method as in Example 1, the entitled compound was obtained.

¹HNMR (300 MHz, DMSO-d₆, δ ppm): 1.53-1.85 (6H, m), 1.90-2.09 (6H, m), 2.55-2.78 (3H, m), 4.95-5.05 (1H, m), 7.95 (4H, s), 9.01 (2H, s); mass spectrum (ESI): 335 (M+H)

Example 8:

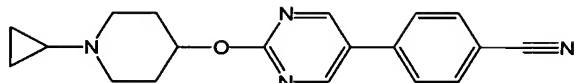


2-(1-cyclohexylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyridine

According to the same method as in Example 1, the entitled compound was obtained.

¹HNMR (300 MHz, DMSO-d₆, δ ppm): 1.15-1.29 (6H, m), 1.60-1.83 (6H, m), 1.97-2.09 (2H, m), 2.25-2.53 (3H, m), 2.77-2.89 (2H, m), 4.95-5.05 (1H, m), 7.96 (2H, s), 9.02 (2H, s); mass spectrum (ESI): 363 (M+H)

Example 9:

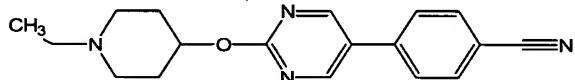


2-(1-cyclopropylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine

According to the same method as in Example 1, the entitled compound was obtained.

¹HNMR (300 MHz, DMSO-d₆, δ ppm): 0.28-0.32 (2H, m), 0.39-0.47 (2H, m), 1.60-1.73 (3H, m), 1.92-2.04 (2H, m), 2.38-2.52 (2H, m), 2.79-2.90 (2H, m), 4.98-5.09 (1H, m), 7.96 (4H, s), 9.01 (2H, s); mass spectrum (ESI): 321 (M+H)

Example 10:

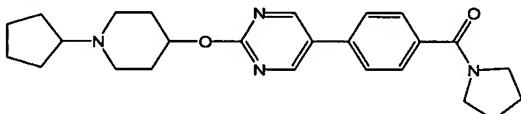


2-(1-ethylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrimidine

According to the same method as in Example 1, the entitled compound was obtained.

¹HNMR (300 MHz, DMSO-d₆, δ ppm): 1.00 (3H, t, J = 7.2 Hz), 1.64-1.76 (2H, m), 1.96-2.08 (2H, m), 2.12-2.24 (2H, m), 2.34 (2H, d, J = 7.2 Hz), 2.69-2.80 (2H, m), 4.96-5.08 (1H, m), 7.96 (4H, s), 9.01 (2H, s); mass spectrum (ESI): 309 (M+H)

Example 11:



2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(pyrrolidin-1-ylcarbonyl)phenyl}pyrimidine

1) Production of 2-(1-cyclopentylpiperidin-4-yloxy)-5-bromopyrimidine:

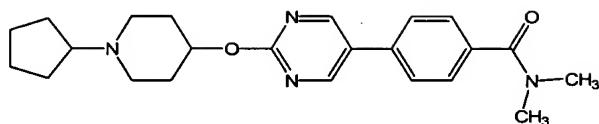
According to the same reaction process as in Example 1-1) but using 2-chloro-5-bromopyrimidine and 4-hydroxy-1-cyclopentylpiperidine, the entitled compound was obtained.

2) 1,2-dimethoxyethane (3.0 ml) and aqueous 2 N sodium carbonate solution (1.0 ml) were added to 2-(1-cyclopentylpiperidin-4-yloxy)-5-bromopyrimidine (176 mg, 0.54 mmol), and then 4-(pyrrolidin-1-ylcarbonyl)phenylboronic acid (142 mg, 0.065 mmol) and tetrakis(triphenylphosphine)palladium(0) (30 mg, 0.026 mmol) were added thereto and stirred in a nitrogen atmosphere at 80°C for 20 hours. The reaction mixture was cooled to room temperature, and water was added to it and extracted with ethyl acetate. The organic layer was washed with saturated saline solution, dried with anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was purified through silica gel column chromatography (C-200, chloroform:methanol = 10:1) to obtain the entitled compound (130 mg, 57 %).

¹HNMR (300 MHz, CDCl₃, δ ppm): 1.35-2.08 (14H, m), 2.08-2.25 (2H, m), 2.35-2.69 (2H, m), 2.82-2.98 (2H, m), 3.42-3.53 (2H, m), 3.60-3.72 (2H, m), 5.06-5.18 (1H, m), 7.55 (2H, d, J = 8.3 Hz), 7.64 (2H, d, J = 8.3 Hz), 8.71 (2H, s); mass spectrum (ESI): 421 (M+H)

According to the same method as in Example 11, the following compounds were obtained.

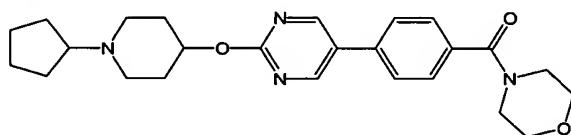
Example 12:



2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(dimethylcarbamoyl)phenyl}pyrimidine

¹HNMR (300 MHz, CDCl₃, δ ppm): 1.45-2.72 (15H, m), 2.85-2.99 (1H, m), 3.04 (3H, brs), 3.14 (3H, brs), 5.08-5.22 (1H, m), 7.51-7.62 (4H, m), 8.72 (2H, s); mass spectrum (ESI): 395 (M+H)

5 Example 13:

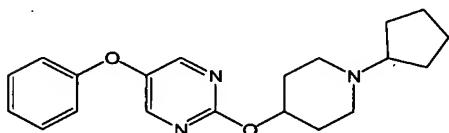


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2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(morpholin-4-ylcarbonyl)phenyl}pyrimidine

¹HNMR (300 MHz, CDCl₃, δ ppm): 1.35-1.81 (6H, m), 1.82-2.22 (6H, m), 2.29-2.65 (3H, m), 2.82-2.98 (2H, m), 3.37-3.99 (8H, m), 5.05-5.18 (1H, m), 7.53 (2H, d, J = 8.2 Hz), 7.57 (2H, d, J = 8.2 Hz), 8.71 (2H, s); mass spectrum (ESI): 437 (M+H)

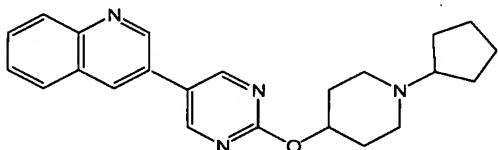
Example 14:



2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(phenoxy)phenyl}pyrimidine

¹HNMR (400 MHz, CDCl₃, δ ppm): 1.50-1.80 (6H, m), 1.86-2.07 (4H, m), 2.16-2.28 (2H, m), 2.52-2.67 (3H, m), 2.89-3.01 (2H, m), 5.02-5.12 (1H, m), 6.93-7.00 (2H, m), 7.10-7.16 (2H, m), 7.30-7.38 (2H, m), 8.27 (2H, s); mass spectrum (ESI): 340 (M+H)

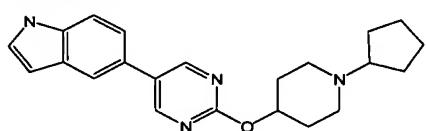
Example 15:



2-(1-cyclopentylpiperidin-4-yloxy)-5-{3-quinolinyl}pyrimidine

¹HNMR (400 MHz, CDCl₃, δ ppm): 1.36-1.77 (6H, m), 1.81-2.04 (4H, m), 2.09-2.21 (2H, m), 2.33-2.47 (2H, m), 2.50-2.61 (1H, m), 2.84-2.97 (2H, m), 5.05-5.18 (1H, m), 7.57-7.63 (1H, m), 7.71-7.78 (1H, m), 7.88 (1H, d, J = 8.1 Hz), 8.13 (1H, d J = 8.4 Hz), 8.25 (1H, d, J = 2.4 Hz), 8.82 (2H, s), 9.07 (1H, d, J = 2.4 Hz); mass spectrum (ESI): 375 (M+H)

Example 16:



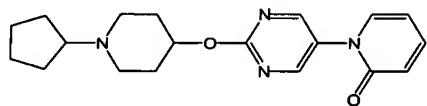
25

2-(1-cyclopentylpiperidin-4-yloxy)-5-{5-indolyl}pyrimidine

¹HNMR (400 MHz, CDCl₃, δ ppm): 1.38-1.80 (6H, m), 1.82-2.06 (4H, m), 2.09-2.23 (2H, m), 2.33-2.65 (3H, m), 2.84-2.99 (2H, m), 5.05-5.18 (1H, m), 6.61 (1H, s), 7.22-7.36 (2H, m), 7.41-7.55 (1H, m), 7.75

(1H, s), 8.35-8.43 (1H, m), 8.72 (2H, s); mass spectrum (ESI): 363 (M+H)

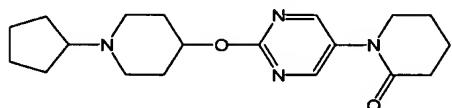
Example 17:



2-(1-cyclopentylpiperidin-4-yloxy)-5-(pyridon-1-yl)pyrimidine

5 ¹HNMR (300 MHz, DMSO-d₆, δ ppm): 1.23-1.84 (10H, m), 1.95-2.06 (2H, m), 2.18-2.28 (2H, m), 2.40-2.55 (1H, m), 2.71-2.82 (2H, m), 4.90-5.02 (1H, m), 6.36 (1H, t, J = 7.0 Hz), 6.50 (1H, d, J = 9.5 Hz), 7.50-7.59 (1H, m), 7.72 (1H, dt, J = 2.0, 7.0 Hz), 8.69 (2H, s); mass spectrum (ESI): 341 (M+H)

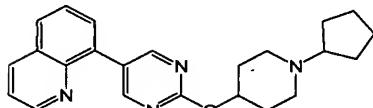
Example 18:



10 2-(1-cyclopentylpiperidin-4-yloxy)-5-(piperidon-1-yl)pyrimidine

¹HNMR (300 MHz, DMSO-d₆, δ ppm): 1.20-2.50 (21H, m), 2.70-2.86 (2H, m), 3.58-3.64 (2H, m), 4.85-4.98 (1H, m), 8.53 (2H, s); mass spectrum (ESI): 345 (M+H)

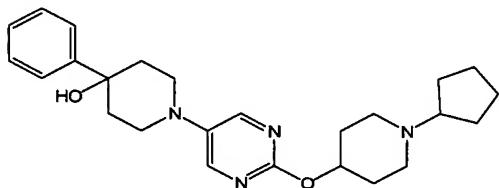
Example 19:



15 2-(1-cyclopentylpiperidin-4-yloxy)-5-{3-quinolinyl}pyrimidine

¹HNMR (400 MHz, CDCl₃, δ ppm): 1.38-1.76 (6H, m), 1.85-2.05 (4H, m), 2.10-2.19 (2H, m), 2.34-2.45 (2H, m), 2.49-2.59 (1H, m), 2.83-2.94 (2H, m), 5.10-5.18 (1H, m), 7.45 (1H, dd, J = 4.0, 8.1 Hz), 7.62 (1H, dd, J = 7.3, 8.1 Hz), 7.72 (1H, dd, J = 1.5, 7.0 Hz), 7.86 (1H, dd, J = 1.5, 8.1 Hz), 8.21 (1H, dd, J = 1.8, 8.1 Hz), 8.86 (2H, s), 8.91 (1H, dd, J = 1.8, 4.4 Hz); mass spectrum (ESI): 375 (M+H)

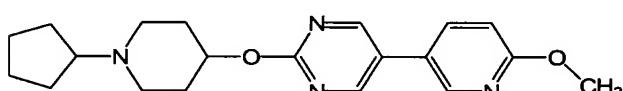
20 Example 20:



2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-phenyl-4-hydroxypiperidin-1-yl)pyrimidine

1 ¹HNMR (400 MHz, CDCl₃, δ ppm): 1.43-1.99 (12H, m), 2.06-2.17 (2H, m), 2.22-2.32 (2H, m), 2.39-2.65 (3H, m), 2.83-2.94 (2H, m), 3.19-3.28 (2H, m), 3.34-3.41 (2H, m), 4.94-5.02 (1H, m), 7.25-7.30 (1H, m), 7.34-7.40 (2H, m), 7.48-7.54 (2H, m), 8.23 (2H, m); mass spectrum (ESI): 423 (M+H)

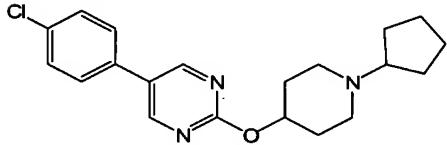
Example 21:



2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-methoxypyridin-5-yl)pyrimidine

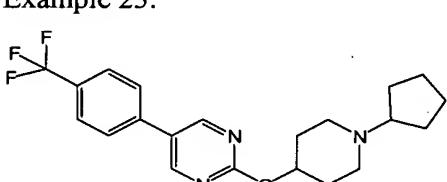
¹HNMR (300 MHz, CDCl₃, δ ppm): 1.46-1.71 (6H, m), 1.85-2.03 (4H, m), 2.14-2.17 (2H, m), 2.45-2.62 (3H, m), 2.90-2.91 (2H, m), 2.90-2.91 (2H, m), 3.97 (3H, s), 5.10-5.11 (1H, m), 6.85 (1H, d, J = 8.6 Hz), 7.69 (1H, dd, J = 2.6, 8.6 Hz), 8.30 (1H, d, J = 2.6 Hz), 8.63 (2H, s); mass spectrum (ESI): 355 (M+H)

5 Example 22:

2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-chlorophenyl)pyrimidine

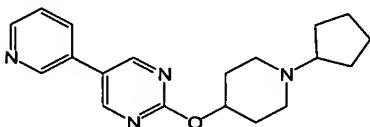
¹HNMR (400 MHz, CDCl₃, δ ppm): 1.38-1.76 (6H, m), 1.84-2.01 (4H, m), 2.07-2.16 (2H, m), 2.32-2.44 (2H, m), 2.49-2.59 (1H, m), 2.82-2.93 (2H, m), 5.03-5.13 (1H, m), 7.43 (4H, s), 8.64 (2H, s); mass spectrum (ESI): 358 (M+H)

10 Example 23:

2-(1-cyclopentylpiperidin-4-yloxy)-5-(3-pyridinyl)pyrimidine

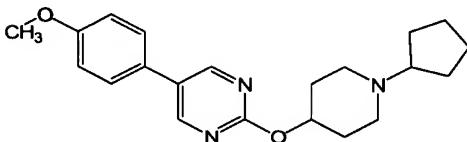
¹HNMR (400 MHz, CDCl₃, δ ppm): 1.39-1.76 (6H, m), 1.84-2.03 (4H, m), 2.07-2.19 (2H, m), 2.33-2.47 (2H, m), 2.51-2.61 (1H, m), 2.83-2.94 (2H, m), 5.05-5.16 (1H, m), 7.61 (2H, d, J = 8.1 Hz), 7.72 (2H, d, J = 8.1 Hz), 8.70 (2H, s); mass spectrum (ESI): 392 (M+H)

Example 24:

2-(1-cyclopentylpiperidin-4-yloxy)-5-(3-pyridinyl)pyrimidine

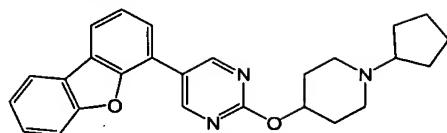
¹HNMR (400 MHz, CDCl₃, δ ppm): 1.36-1.76 (6H, m), 1.84-2.01 (4H, m), 2.07-2.17 (2H, m), 2.31-2.43 (2H, m), 2.49-2.59 (1H, m), 2.83-2.94 (2H, m), 5.06-5.15 (1H, m), 7.37-7.43 (1H, m), 7.78-7.83 (1H, m), 8.61-8.66 (1H, m), 8.69 (2H, s), 8.75-8.80 (1H, m); mass spectrum (ESI): 325 (M+H)

Example 25:

2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-methoxyphenyl) pyrimidine

¹HNMR (400 MHz, CDCl₃, δ ppm): 1.37-1.75 (6H, m), 1.84-2.00 (4H, m), 2.06-2.16 (2H, m), 2.32-2.43 (2H, m), 2.49-2.59 (1H, m), 2.82-2.93 (2H, m), 3.85 (3H, s), 5.02-5.10 (1H, m), 6.99 (2H, d, J = 8.8 Hz), 7.42 (2H, d, J = 8.8 Hz), 8.63 (2H, s); mass spectrum (ESI): 354 (M+H)

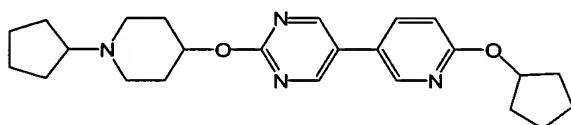
Example 26:

2-(1-cyclopentylpiperidin-4-yloxy)-5-(dibenzofuran-4-yl)pyrimidine

¹HNMR (400 MHz, CDCl₃, δ ppm): 1.38-1.77 (6H, m), 1.85-2.05 (4H, m), 2.11-2.21 (1H, m), 2.34-2.46

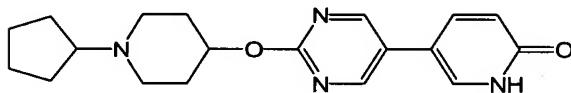
5 (2H, m), 2.51-2.61 (1H, m), 2.86-2.97 (2H, m), 5.10-5.20 (1H, m), 7.34-7.60 (5H, m), 7.94-8.00 (2H, m), 9.04 (2H, s); mass spectrum (ESI): 414 (M+H)

Example 27:

2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-cyclopentyloxypyridin-5-yl)pyrimidine

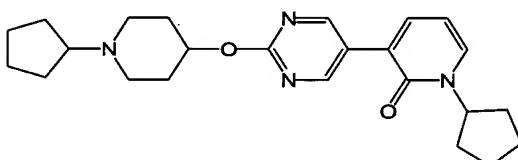
10 ¹HNMR (300 MHz, CDCl₃, δ ppm): 1.47-2.17 (20H, m), 2.46-2.52 (3H, m), 2.89-2.92 (2H, m), 5.11-5.12 (1H, m), 5.40-5.44 (1H, m), 6.78 (1H, d, J = 8.6 Hz), 7.68 (1H, dd, J = 2.6, 8.6 Hz), 8.29 (1H, d, J = 2.6 Hz), 8.63 (2H, s); mass spectrum (ESI): 409 (M+H)

Example 28:

2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-pyridon-5-yl)pyrimidine

¹HNMR (300 MHz, CDCl₃, δ ppm): 1.43-1.76 (6H, m), 1.84-2.00 (4H, m), 2.11-2.17 (2H, m), 2.39-2.48 (2H, m), 2.56-2.61 (1H, m), 2.87-2.90 (2H, m), 5.07-5.10 (1H, m), 6.73 (1H, d, J = 9.5 Hz), 7.55 (1H, d, J = 2.2 Hz), 7.66 (1H, dd, J = 2.3, 9.3 Hz), 8.56 (2H, s); mass spectrum (ESI): 341 (M+H)

Example 29:



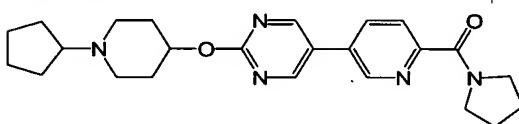
20

2-(1-cyclopentylpiperidin-4-yloxy)-5-(1-cyclopentyl-2-pyridon-3-yl)pyrimidine

According to the same method as in Example 27, the entitled compound was obtained.

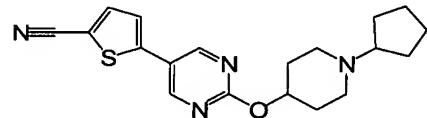
¹HNMR (300 MHz, CDCl₃, δ ppm): 1.42-1.99 (16H, m), 2.09-2.25 (4H, m), 2.42-2.59 (3H, m), 2.81-2.91 (2H, m), 5.08-5.11 (1H, m), 5.33-5.38 (1H, m), 6.31 (1H, t, J = 6.9 Hz), 7.37-7.44 (2H, m), 8.83 (2H, s); mass spectrum (ESI): 409 (M+H)

Example 30:

2-(1-cyclopentylpiperidin-4-yloxy)-5-{2-(pyrrolidin-1-ylcarbonyl)pyridin-5-yl}pyrimidine

¹HNMR (300 MHz, CDCl₃, δ ppm): 1.40-2.35 (16H, m), 2.35-2.75 (3H, m), 2.85-3.00 (2H, m), 3.66-3.75 (2H, m), 3.75-3.88 (2H, m), 5.08-5.22 (1H, m), 7.93 (2H, dd, J = 2.2, 8.1 Hz), 8.00 (1H, d, J = 8.1 Hz), 8.74 (2H, s), 8.75 (1H, d, J = 2.2 Hz); mass spectrum (ESI): 422 (M+H)

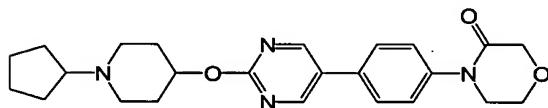
Example 31:



2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-cyano-5-thenyl)pyrimidine

¹HNMR (400 MHz, CDCl₃, δ ppm): 1.38-1.78 (6H, m), 1.83-2.01 (4H, m), 2.07-2.18 (2H, m), 2.34-2.47 (2H, m), 2.51-2.62 (1H, m), 2.83-2.93 (2H, m), 5.06-5.14 (1H, m), 7.23 (1H, d, J = 4.0 Hz), 7.62 (1H, d, J = 4.0 Hz), 8.69 (2H, s); mass spectrum (ESI): 355 (M+H)

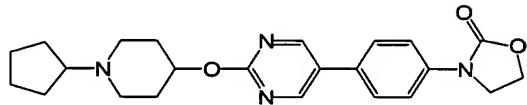
10 Example 32:



2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(3-oxomorpholin-1-yl)phenyl}pyrimidine

¹HNMR (300 MHz, CDCl₃, δ ppm): 1.38-2.08 (12H, m), 2.15-2.35 (1H, m), 2.48-2.82 (2H, m), 2.88-3.05 (2H, m), 3.76-3.85 (2H, m), 4.03-4.12 (2H, m), 4.38 (2H, s), 5.08-5.27 (1H, m), 7.47 (2H, d, J = 8.5 Hz), 7.57 (2H, d, J = 8.5 Hz), 8.70 (2H, s); mass spectrum (ESI): 423 (M+H)

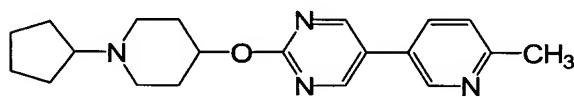
15 Example 33:



2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(2-oxazolidinon-3-yl)phenyl}pyrimidine

¹HNMR (300 MHz, CDCl₃, δ ppm): 1.37-2.12 (12H, m), 2.12-2.33 (1H, m), 2.43-2.80 (2H, m), 2.85-3.03 (2H, m), 4.11 (2H, t, J = 7.9 Hz), 4.54 (2H, t, J = 7.9 Hz), 5.08-5.24 (1H, m), 7.53 (2H, d, J = 8.4 Hz), 7.68 (2H, d, J = 8.4 Hz), 8.69 (2H, s); mass spectrum (ESI): 409 (M+H)

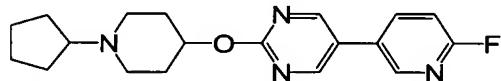
20 Example 34:



2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-methyl-3-pyridin-5-yl)pyrimidine

25 ¹HNMR (300 MHz, CDCl₃, δ ppm): 1.39-1.69 (6H, m), 1.83-2.00 (4H, m), 2.09-2.14 (2H, m), 2.33-2.40 (2H, m), 2.51-2.56 (1H, m), 2.61 (3H, s), 2.86-2.90 (2H, m), 5.07-5.10 (1H, m), 7.23-7.27 (1H, m), 7.70 (1H, dd, J = 2.4, 8.0 Hz), 8.55-8.67 (3H, m); mass spectrum (ESI): 339 (M+H)

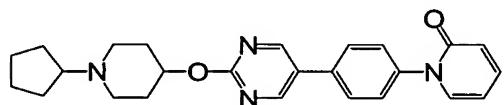
Example 35:



30 2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-fluoro-3-pyridin-5-yl)pyrimidine

¹HNMR (300 MHz, CDCl₃, δ ppm): 1.39-2.00 (10H, m), 2.09-2.15 (2H, m), 2.34-2.40 (2H, m), 2.52-2.57 (1H, m), 2.87-2.88 (2H, m), 5.08-5.13 (1H, m), 7.06 (1H, dd, J = 3.0, 8.5 Hz), 7.92 (2H, dt, J = 2.6, 8.4 Hz), 8.37 (1H, d, J = 1.9 Hz), 8.56 (2H, s); mass spectrum (ESI): 343 (M+H)

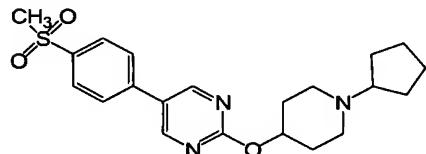
Example 36:



2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(2-pyridon-1-yl)phenyl}pyrimidine

¹HNMR (300 MHz, CDCl₃, δ ppm): 1.38-2.05 (10H, m), 2.05-2.23 (2H, m), 2.29-2.65 (2H, m), 2.81-3.00 (2H, m), 5.01-5.20 (1H, m), 6.29 (1H, t, J = 6.7 Hz), 6.69 (1H, d, J = 9.2 Hz), 7.32-7.48 (2H, m), 7.52 (2H, d, J = 8.3 Hz), 7.64 (2H, d, J = 8.3 Hz), 8.73 (2H, s); mass spectrum (ESI): 417 (M+H)

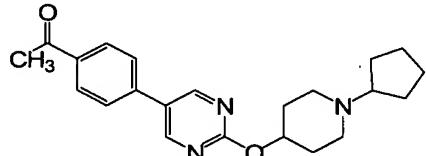
10 Example 37:



2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(methylsulfonyl)phenyl}pyrimidine

¹HNMR (400 MHz, CDCl₃, δ ppm): 1.38-1.77 (6H, m), 1.84-2.04 (4H, m), 2.08-2.19 (2H, m), 2.31-2.47 (2H, m), 2.50-2.61 (1H, m), 2.83-2.97 (2H, m), 5.06-5.16 (1H, m), 7.71 (2H, dd, J = 2.2, 6.6 Hz), 8.05 (2H, dd, J = 1.8, 6.6 Hz), 8.73 (2H, s); mass spectrum (ESI): 402 (M+H)

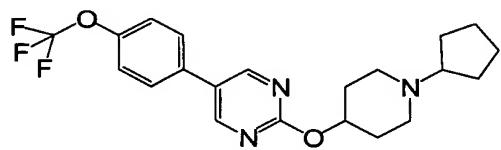
15 Example 38:



2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-acetylphenyl}pyrimidine

¹HNMR (400 MHz, CDCl₃, δ ppm): 1.38-1.76 (6H, m), 1.84-2.02 (4H, m), 2.07-2.17 (2H, m), 2.32-2.44 (2H, m), 2.49-2.60 (1H, m), 2.64 (3H, s), 2.83-2.94 (2H, m), 5.06-5.15 (1H, m), 7.61 (2H, d, J = 8.1 Hz), 8.05 (2H, d, J = 8.1 Hz), 8.73 (2H, s); mass spectrum (ESI): 366 (M+H)

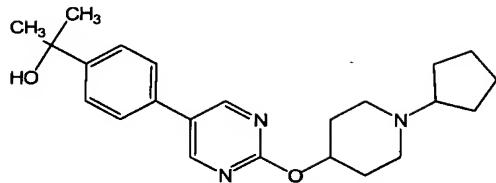
20 Example 39:



2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-trifluoromethoxyphenyl)pyrimidine

¹HNMR (400 MHz, CDCl₃, δ ppm): 1.38-1.76 (6H, m), 1.83-2.01 (4H, m), 2.03-2.17 (2H, m), 2.31-2.44 (2H, m), 2.49-2.59 (1H, m), 2.81-2.93 (2H, m), 5.05-5.14 (1H, m), 7.32 (2H, d, J = 8.8 Hz), 7.51 (2H, d, J = 8.8 Hz), 8.65 (2H, s); mass spectrum (ESI): 408 (M+H)

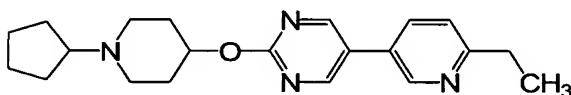
25 Example 40:



2-(1-cyclopentylpiperidin-4-yloxy)-5-{4-(2-hydroxy-2-propyl)phenyl}pyrimidine

¹HNMR (400 MHz, CDCl₃, δ ppm): 1.38-1.77 (6H, m), 1.83-2.07 (4H, m), 2.07-2.18 (2H, m), 2.34-2.47 (2H, m), 2.51-2.61 (1H, m), 2.82-2.96 (2H, m), 5.03-5.16 (1H, m), 7.47 (2H, dd, J = 2.2, 6.6 Hz), 7.59 (2H, dd, J = 2.2, 6.6 Hz), 8.67 (2H, s); mass spectrum (ESI): 382 (M+H)

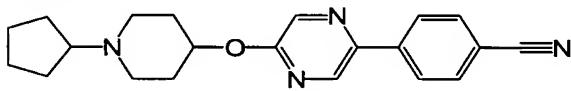
5 Example 41:



2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-ethyl-5-pyridyl)pyrimidine

¹HNMR (300 MHz, CDCl₃, δ ppm): 1.31-1.69 (9H, m), 1.84-2.00 (4H, m), 2.09-2.14 (2H, m), 2.33-2.37 (2H, m), 2.51-2.57 (1H, m), 2.85-2.92 (4H, m), 5.08-5.11 (1H, m), 7.26-7.29 (1H, m), 7.73 (2H, dd, J = 2.4, 8.1 Hz), 8.67-8.68 (3H, m); mass spectrum (ESI): 353 (M+H)

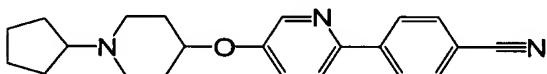
10 Example 42:



2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyrazine

¹HNMR (300 MHz, CDCl₃, δ ppm): 1.42-1.62 (4H, m), 1.67-1.94 (6H, m), 2.08-2.13 (2H, m), 2.33-2.39 (2H, m), 2.52-2.57 (1H, m), 2.85-2.88 (2H, m), 5.09-5.12 (1H, m), 7.75 (2H, d, J = 8.7 Hz), 8.03 (2H, d, J = 8.7 Hz), 8.27 (1H, d, J = 1.4 Hz), 8.52 (1H, d, J = 1.4 Hz); mass spectrum (ESI): 349 (M+H)

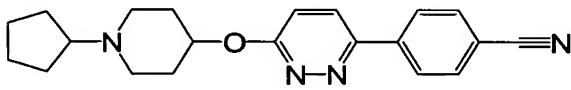
15 Example 43:



20 5-(1-cyclopentylpiperidin-4-yloxy)-2-(4-cyanophenyl)pyridine

¹HNMR (300 MHz, CDCl₃, δ ppm): 1.39-1.73 (6H, m), 1.84-1.94 (4H, m), 2.03-2.10 (2H, m), 2.33-2.39 (2H, m), 2.52-2.57 (1H, m), 2.81-2.83 (2H, m), 4.41-4.44 (1H, m), 7.26-7.31 (1H, m), 7.68-7.74 (3H, m), 8.05 (2H, d, J = 8.2 Hz), 8.40 (1H, d, J = 2.9 Hz); mass spectrum (ESI): 348 (M+H)

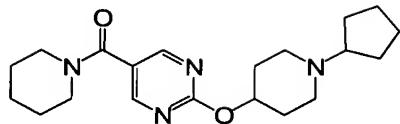
Example 44:



2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-cyanophenyl)pyridazine

¹HNMR (300 MHz, CDCl₃, δ ppm): 1.51-1.76 (6H, m), 1.88-2.04 (4H, m), 2.17-2.33 (2H, m), 2.48-2.72 (3H, m), 2.96-3.02 (2H, m), 5.42-5.46 (1H, m), 7.08 (1H, d, J = 9.3 Hz), 7.78-7.84 (3H, m), 8.13 (1H, d, J = 8.2 Hz); mass spectrum (ESI): 349 (M+H)

25 30 Example 45:



2-(1-cyclopentylpiperidin-4-yloxy)-5-(piperidin-1-ylcarbonyl)pyrimidine

1) Production of 2-(1-t-butoxycarbonylpiperidin-4-yloxy)-5-(phenoxy carbonyl)pyrimidine:

Palladium acetate (35 mg, 0.31 mmol), bis(diphenylphosphino)ferrocene (170 mg, 1.54 mmol), phenol (1.5 ml, 17.1 mmol), triethylamine (0.5 ml, 3.6 mmol) were added in that order to a toluene solution (1.0 ml) of 2-(1-t-butoxycarbonylpiperidin-4-yloxy)-5-bromopyridine (550 mg, 1.54 mmol), and stirred in a carbon monoxide atmosphere under normal pressure at 100°C for 14 hours. The reaction mixture was cooled to room temperature, an aqueous saturated sodium bicarbonate solution was added thereto and extracted with ethyl acetate. The organic layer was washed with saturated saline solution, dried with anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was purified through silica gel column chromatography (C-200, hexane:ethyl acetate = 7:3) to obtain the entitled compound (589 mg, 96 %).

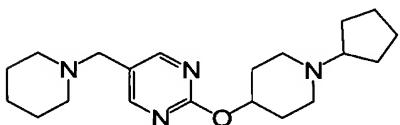
2) Production of 2-(1-t-butoxycarbonylpiperidin-4-yloxy)-5-(piperidin-1-carbonyl)pyrimidine:

Piperidine (0.02 ml, 0.20 mmol) was added to a dimethylformamide solution (1.0 ml) of 2-(1-t-butoxycarbonylpiperidin-4-yloxy)-5-(phenoxy carbonyl)pyrimidine (40 mg, 0.100 mmol), and stirred at room temperature for 12 hours. Water was added to the reaction mixture and extracted with ethyl acetate. The organic layer was washed with saturated saline solution, dried with anhydrous magnesium sulfate, and concentrated under reduced pressure. The residue was purified through partitioning thin-layer chromatography (hexane:ethyl acetate = 3:7) to obtain the entitled compound (38 mg, 97 %).

3) According to the same method as in Example 1-3), 4) but using 2-(1-t-butoxycarbonylpiperidin-4-yloxy)-5-(piperidin-1-carbonyl)pyrimidine (38 mg, 0.100 mmol), the entitled compound was obtained (17 mg, 43 %).

¹HNMR (400 MHz, CDCl₃, δ ppm): 1.35-1.99 (20H, m), 2.03-2.15 (2H, m), 2.30-2.42 (2H, m), 2.48-2.58 (1H, m), 2.80-2.91 (2H, m), 5.02-5.14 (1H, m), 8.56 (2H, s); mass spectrum (ESI): 359 (M+H)

Example 46:



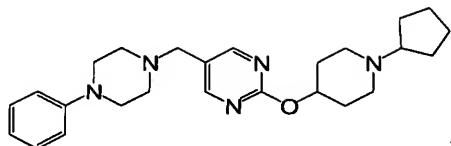
2-(1-cyclopentylpiperidin-4-yloxy)-5-(piperidin-1-ylmethyl)phenyl pyrimidine

The compound of Example 45 was reduced with aluminium lithium hydride and post-processed according to an ordinary method, and the resulting residue was purified through partitioning thin-layer chromatography (chloroform:methanol = 10:1) to obtain the entitled compound (30 mg, 65 %).

¹HNMR (400 MHz, CDCl₃, δ ppm): 1.33-2.12 (18H, m), 2.27-2.42 (6H, m), 2.46-2.57 (1H, m), 2.80-2.92 (2H, m), 3.36 (2H, s), 4.95-5.05 (1H, m), 8.37 (2H, s); mass spectrum (ESI): 345 (M+H)

According to the same method as in Example 46, the following compounds were obtained.

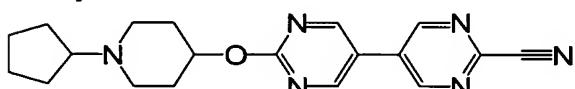
35 Example 47:



2-(1-cyclopentylpiperidin-4-yloxy)-5-(4-phenylpiperazin-1-ylmethyl)pyrimidine

¹HNMR (400 MHz, CDCl₃, δ ppm): 1.37-1.97 (10H, m), 2.04-2.13 (2H, m), 2.31-2.42 (2H, m), 2.48-2.63 (5H, m), 2.81-2.91 (2H, m), 3.14-3.21 (4H, m), 3.47 (2H, s), 4.98-5.08 (1H, m), 6.80-6.92 (3H, m), 7.20-7.27 (2H, m), 8.43 (2H, s); mass spectrum (ESI): 422 (M+H)

5 Example 48:



2-(1-cyclopentylpiperidin-4-yloxy)-5-(2-cyanopyrimidin-4-yl)pyrimidine

10 1) Production of 2-(1-t-butoxycarbonylpiperidin-4-yloxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxabororan-2-yl)pyrimidine:

Bis(pinacholato)diboron (160 mg, 0.63 mmol), bis(diphenylphosphino)ferrocene-palladium(II) dichloride, dichloromethane (14 mg, 0.017 mmol), potassium acetate (165 mg, 1.68 mmol) were added to a dimethylsulfoxide (4.0 ml) solution of 2-(1-t-butoxycarbonylpiperidin-4-yloxy)-5-bromopyrimidine (200 mg, 0.56 mmol), and stirred in a nitrogen atmosphere at 80°C for 1 hour. The reaction mixture was cooled to room temperature, and extracted with ethyl acetate. The organic layer was washed with water and saturated saline solution, dried with anhydrous sodium sulfate and concentrated under reduced pressure. The residue was purified through silica gel column chromatography (C-300, chloroform:methanol= 100:3) to obtain the entitled compound (86 mg, 38 %).

15 2) Production of 2-(1-t-butoxycarbonylpiperidin-4-yloxy)-5-(2-cyanopyrimidin-5-yl)pyrimidine:

20 2-Cyano-5-bromopyrimidine (20 mg, 0.11 mmol), bis(diphenylphosphino)ferrocene-palladium(II) dichloride, dichloromethane (4.0 mg, 0.005 mmol), potassium phosphate (53 mg, 0.25 mmol) were added to a dimethylformamide (2.0 ml) solution of 2-(1-t-butoxycarbonylpiperidin-4-yloxy)-5-(4,4,5,5-tetramethyl-1,3,2-dioxabororan-2-yl)pyrimidine (20 mg, 0.049 mmol), and stirred in a nitrogen atmosphere at 80°C for 1 hour. The reaction mixture was cooled to room temperature, and extracted with ethyl acetate. The organic layer was washed with water, saturated sodium bicarbonate solution and saturated saline solution in that order, dried with anhydrous sodium sulfate and concentrated under reduced pressure. The residue was purified through partitioning thin-layer column chromatography (ethyl acetate:hexane = 1:1) to obtain the entitled compound (9.3 mg, 49 %).

25 30 3) 2-(1-t-butoxycarbonylpiperidin-4-yloxy)-5-(2-cyanopyrimidin-5-yl)pyrimidine (9.3 mg, 0.024 mmol) was processed in the same manner as in Example 1-3), 4) to obtain the entitled compound (4.5 mg, 53 %).

¹HNMR (300 MHz, DMSO-d₆, δ ppm): 1.40-1.80 (6H, m), 1.86-2.08 (4H, m), 2.09-2.22 (2H, m), 2.35-2.52 (2H, m), 2.52-2.65 (1H, m), 2.86-2.98 (2H, m), 5.12-5.21 (1H, m), 8.78 (2H, s), 9.03 (2H, s); mass spectrum (ESI): 351 (M+H)

INDUSTRIAL APPLICABILITY

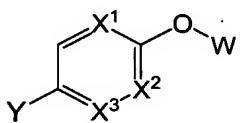
The heteroaryloxy-nitrogen-containing saturated heterocyclic derivatives of formula (I) and their pharmaceutically-acceptable salts of the invention have a strong histamine-H3 receptor agonistic or inverse-agonistic activity, and are useful for remedy and/or prevention of metabolic system diseases such as obesity, diabetes, hormone secretion disorder, hyperlipemia, gout, fatty liver; circulatory system diseases, for example, stenocardia, acute/congestive cardiac insufficiency, cardiac infarction, coronary arteriosclerosis, hypertension, nephropathy, and central and peripheral nervous system diseases such as bulimia, emotional disorder, melancholia, anxiety, epilepsy, delirium, dementia, shinzophrenia, attention deficit/hyperactivity disorder, memory disorder, Alzheimer's disease, Parkinson's disease, sleep disorder, recognition disorder, motion disorder, paresthesia, dysosmia, epilepsy, morphine resistance, narcotic dependency, alcoholic dependency.

[Designation of Document] Abstract

[Abstract]

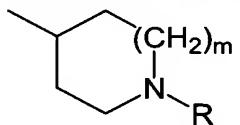
[Problem] To Provide the compounds having a histamine-H3 receptor antagonistic or inverse-agonistic activity and are useful for remedy and/or prevention of obesity, diabetes, hormone secretion disorders, sleep disorders, etc.

5 [Means for Solution] The compounds of a formula (I) and their pharmaceutically-acceptable salts:



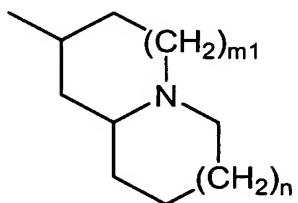
(I)

wherein X1, X2 and X3 each independently represent N or CH; W represents the following formula (II):



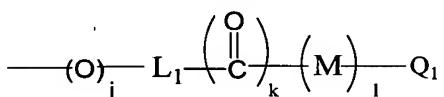
(II)

or the following formula (III):



(III)

Y represents a group of a formula (IV):



(IV)